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Decision Making Mechanisms in the Human Brain: The case of the decision threshold.

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Dedicated to my family: for their love, patience, and support!

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Kurzfassung

In dieser Arbeit habe ich Mechanismen des menschlichen Gehirns untersucht, die zur Anpassung des Entscheidungskriteriums führen.

Bei Wahrnehmungsentscheidungen, wie z.B. dem Erkennen der Bewegungsrichtung eines Objekts (z.B. nach links oder rechts), wird aufgrund theoretischer und empirischer Befunde angenommen, dass sensorische Information kontinuierlich bis zur Überschreitung eines Entscheidungskriteriums gesammelt wird. Dieser Prozess lässt sich durch theoretische Modelle, sogenannte Akkumulatormodelle, mathematisch beschreiben. Aufgrund umfangreicher Verhaltensdaten, neurophysiologischer und bildgebender Befunde, wird angenommen, dass diese Modelle den zugrundeliegenden Informationsverarbeitungsprozess im Gehirn sehr gut abbilden. Ein zentraler Parameter dieser Modelle ist dabei das Entscheidungskriterium, weil es den Entscheidungsprozess determiniert.

In dieser Dissertation werden zwei Projekte diskutiert, in denen neuronale Mechanismen des Entscheidungskriteriums von mir untersucht wurden.

Zentral im ersten Projekt ist die Frage nach dem neuronalen Mechanismus der Anpassung des Entscheidungskriteriums (engl. decision threshold modulation). Ausgehend von einem biophysikalischen Modell das den erwähnten Entscheidungsprozess in einem Neuronalen Netz implementiert, untersuchte ich die Veränderbarkeit des Entscheidungskriteriums. In dem Neuronalen Netz wird das Entscheidungskriterium durch die Anpassung von Interaktionen zwischen Kortikalen Akkumulator- (engl. integrator) und Striatalen Neuronen moduliert. Unter Anwendung bildgebender Verfahren und komputationaler Modelle konnte ich zeigen, dass das Entscheidungskriterium durch die Modulation von Interaktionen, zwischen Hirnregionen, die für eine Entscheidung relevant sind, angepasst wird.

Akkumulatormodelle lassen sich theoretisch aus statistischen Tests über optimales Entscheiden herleiten. Ausgehend von einem komputationalen Modell über optimales Entscheiden in kortiko-basalganglionischen Netzwerken, habe ich im zweiten Projekt untersucht, wie der Nucleus subthalamicus (engl. STN, Subthalamic Nucleus), der in diesem Modell eine

zentrale Rolle bei Entscheidungen spielt, bei einfachen, perzeptuellen Entscheidungen das Entscheidungskriterium beeinflusst. Dazu nutzte ich die Möglichkeit der Tiefenhirnstimulation (engl. DBS, Deep Brain Stimulation) des STN bei Parkinson Patienten. In dieser Studie konnte ich die Modellannahmen über die Funktion des STN bestätigen. Ebenso konnte ich zeigen, dass die DBS des STN die Modulation des Entscheidungskriteriums einschränkt.

Zusammengefasst zeigt meine Dissertation erstens, dass das Entscheidungskriterium durch eine Veränderung in der Kopplung zwischen Kortikalen und Subkortikalen Hirnsystemen moduliert wird und zweitens, das diese Anpassung durch Signale des STN beeinflusst wird.

Schlagwörter: *Perzeptuelle Entscheidungsfindung, Entscheidungskriterium, Akkumulatormodell*

Abstract Summary

This thesis investigates the neural basis of the decision threshold. The neural basis of decision making is one of the most central topics in cognitive and systems neuroscience. The ultimate goal of this research is to provide a complete account of the mechanisms and neural substrates underlying our ability to make choices in complex and ever-changing environments. Perceptual decision making has previously been described as the continuous accumulation of noisy sensory evidence in the brain until a decision criterion or threshold is reached. A decision threshold ultimately determines the decision process by balancing evidence accumulation and deliberation time in order to appropriately select an action.

Let us consider a simplified scenario in which foragers sample the environment for available patches of food. When plentiful resources are available, foragers should thoroughly examine and thus deliberately choose rich patches over empty patches to maximize reward. Compare this to a situation where resources have been nearly exploited. Now, decisions about which patch to choose have to happen quickly as foragers compete for the remaining resources. While these two situations differ in their incentive structure, they do share a common component. The forager adjusts her decision criterion in each situation that would appropriately address the change in circumstances.

Whereas accumulation of sensory evidence has been extensively researched having acquired a substantial body of knowledge, the mechanisms of the flexible decision threshold remain poorly understood. Hence, motivated by compelling theoretical frameworks - such as the sequential sampling framework of decision making - I have investigated mechanisms of the decision threshold during perceptual decision making.

In the first project, I investigated the neural mechanism of decision threshold modulation for reward maximization in a direction of motion discrimination task. By combining functional MRI (fMRI) with computational models of perceptual decision making, i.e. the drift diffusion model (DDM), it can be shown that modulation of the decision threshold is achieved by adjusting the

effective connectivity within cortico-striatal and cerebellar-striatal brain systems. This change-in-connectivity mechanism, which has the effect of balancing different decision relevant sources of information, reflects a central aspect of decision making.

Most importantly, a modulation of the decision threshold influences performance: a lower threshold leads to faster but also less accurate decision and vice versa. It has been theoretically shown that sequential sampling models, especially the drift-diffusion model can adjust the decision threshold in an optimal way for simple forms of decision making. Optimality under these conditions is defined as the optimal trade-off between decision time and performance accuracy. Notably, in these decision situations, time for deliberation and error rate are negatively related. The model can minimize decision time for a specified performance level. As a consequence, this notion of optimality has potential implications for formulations of information processes explaining perceptual decision making.

In the second project, I investigated neurocomputational models of optimal decision making via cortico-basal ganglia circuitry to investigate this feature in detail. These models have ascribed a crucial computational role to the subthalamic nucleus (STN) and are (mathematically) equivalent to the models used in the first study. In this project, participants suffering from Parkinson's disease (PD) were also asked to perform a motion discrimination task. Here we used a combination of psychophysics, neurostimulation and computational modeling and probed perceptual decision making under a) different states of deep brain stimulation (DBS) of the subthalamic nucleus (STN) and b) changing response instructions. The results indicate that DBS of the STN significantly influences a) performance for perceptual judgments under high decision conflict, and b) the magnitude of decision criterion adjustment. These findings are of particular interest, as they demonstrate on an individual basis that STN computation is crucial for an optimal balance between competing decision demands.

Taken together, I investigated mechanisms of the decision threshold and showed that the modulation of a threshold for perceptual decision making is

instantiated by a change in connectivity between cortio-striatal and cerebellar-striatal brain systems. In addition, I demonstrated that the optimal adjustment of the decision threshold is likely to be based on computations by the STN. Together these findings advance the idea of the decision threshold as a general mechanism for decision making and shed light on the neural mechanisms implementing it.

Keywords: *Decision making, perception, decision threshold, sequential sampling*

List of original publication

This thesis is based on the following original research articles:

Project I

Green, N., Biele, G.P., Heekeren, H.R. (2012)

Changes in neural connectivity underlie decision threshold modulation for reward maximization. J Neurosci, 32(43):14942-50.

http://dx.doi.org/10.1523/JNEUROSCI.0573-12.2012

Project II

Green, N., Bogacz, R., Hübl, J., Beyer, A-K.., Kühn, A.A., Heekeren, H.R. (in revision).

Deep Brain Stimulation of the subthalamic nucleus reduces the influence of conflict in perceptual decision making.

List of Abbreviations

BOLD	Blood Oxygenation Level Dependent
CPP	Centro-Parietal Positivity
DBS	Deep Brain Stimulation
DDM	Drift Diffusion Model
DLPFC	Dorsolateral Prefrontal Cortex
EEG	Electroencephalography
ER	Error Rate
FEF	Frontal Eye Field
FFA	Fusiform Face Area
fMRI	Functional Magnetic Resonance Imaging
GP	Globus Pallidus
IFC	Inferior Frontal Cortex
IPS	Intraparietal Sulcus
LIP	Lateral Interparietal Cortex
(M)SPRT	(Multi-Hypothesis) Sequential Probability Ratio Test
PD	Parkinson's Disease
PMv	Ventral Premotor Cortex
PPA	Parahippocampal Place Area
RDT	Random Dot Stimulus
rmANOVA	Repeated Measurements Analysis of Variance
RT	Reaction Time
SAT	Speed Accuracy Trade-off
SI	Primary Somatosensory Cortex
STN	Subthalamic Nucleus
TMS	Transcranial Magnetic Stimulation

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1. Introduction

Decision making is a central cognitive function. We gather information, we are in a certain emotional state, we value choice alternatives and we remember previous experiences and weigh possible options based on (in)complete knowledge in many everyday decisions. Choosing a course of action or thought - based on the aforementioned aspects - eventually allows us to commit to one choice or another, enabling us to interact appropriately with the world.

Decision Making is an extensive research topic spanning many disciplines such as biology, computer science, economics, engineering, psychology, and neuroscience, to name but a few (von Neumann and Morgenstern, 1944; Wald, 1945; Newell, 1972; Tversky and Kahneman, 1981; Platt and Glimcher, 1999; Gold and Shadlen, 2007, Heekeren et al., 2008; Rangel et al., 2008; Bach and Dolan, 2012).

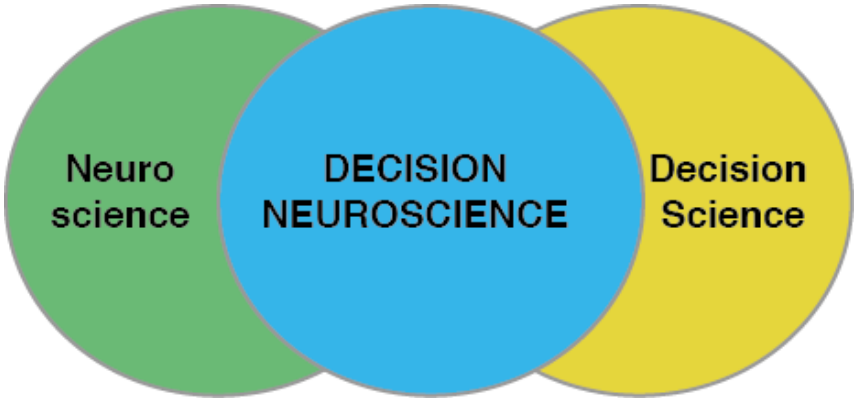

Figure 1. ***Decision Neuroscience.***
The combination of decision sciences such as psychology, computational sciences and economics with neuroscience in order to acquire one coherent framework of neural decision making mechanisms.

Decision neuroscience, the neuroscientific and decision theoretic research of decision making is particularly successful in enhancing interdisciplinary research on decision making across disciplinary boundaries (Figure 1). For instance in the case of neuroeconomics it combines concepts and methods from economics, psychology and neuroscience (Glimcher and Rustichini, 2004; Mohr et al., 2010; Levallois et al., 2012). In the case of computational

psychiatry and ageing it spans fields such as ageing, cognitive science, computational neuroscience, psychology, and psychiatry (Thagard, 2008; Li et al., 2008; Montague et al, 2012).

The understanding of the neural mechanisms and systems underlying simple forms of decision making – such as in perceptual decision making - together with concepts and methods from disciplines such as psychology, economics, and computational sciences help to generate explanatory rich and detailed theories that span different levels of analysis (van Hemmen and Sejnowski, 2005). One very coherent formulation of this idea, has been put forward by David Marr (Marr, 1983). Studying the visual system, he proposed a model-based approach for thinking about the brain in terms of a complex information processing system, which encompasses three distinct but complementary levels of analysis:

1. The computational level, which considers the goal of the system.
2. The algorithmic level, which considers the representations and processes that the system uses to achieve these goals.
3. The implementational level, which considers how these processes are physically realized.

Following this schema I investigated mechanisms of the decision threshold during simple forms of decision making in the human brain. A decision threshold ultimately determines the decision process by balancing evidence accumulation and deliberation in order to appropriately select an action (Diederich and Busemeyer, 2006; Simen et al., 2006; Lo and Wang, 2006). Thus this mechanism allows decision makers to flexibly adapt to different demands of the decision environment (cf. Chittka et al., 2009; Castellano and Carmelli, 2011).

Inspired by the sequential sampling framework of decision making as well as substantial behavioral and neural empirical findings thereof (Smith and Ratcliff, 2004; Gold and Shadlen, 2007), I applied computational models implementing the decision threshold as a central parameter: such as the drift diffusion model (Ratcliff and McKoon, 2008) in order to map it to neural processes and structures (cf. Forstmann et al., 2011). According to the

sequential sampling framework of decision making, sensory-based decisions are formed, by accumulating noisy sensory information until a decision boundary or threshold is crossed (Smith and Ratcliff, 2004; Kiani et al., 2006).

Marr's framework can thus be applied to my research question as follows:

The computational and algorithmic levels, in the context of this thesis, refer to a correct (and optimal) perceptual categorization (i.e. is it a face or a house that I see). For instance, sequential sampling models instantiate the algorithmic level of perceptual decisions. It is assumed that a perceptual decision is made, by integrating evidence over time until a decision threshold is crossed. Finally, the physical level refers to the neural mechanisms and neural systems that implement decision processes.

In the following sections I will review the theoretical and empirical foundations of this dissertation beginning with the discussion of perceptual decision making. Subsequently I will introduce phenomenological models of perceptual decision making, namely variants of the sequential sampling framework. Before I describe the research projects in detail, I will state the main research questions of this thesis, which concern neural mechanisms of the decision threshold. Lastly, I will discuss the findings, their implications and propose open questions that are important for future research.

2. Perceptual Decision Making

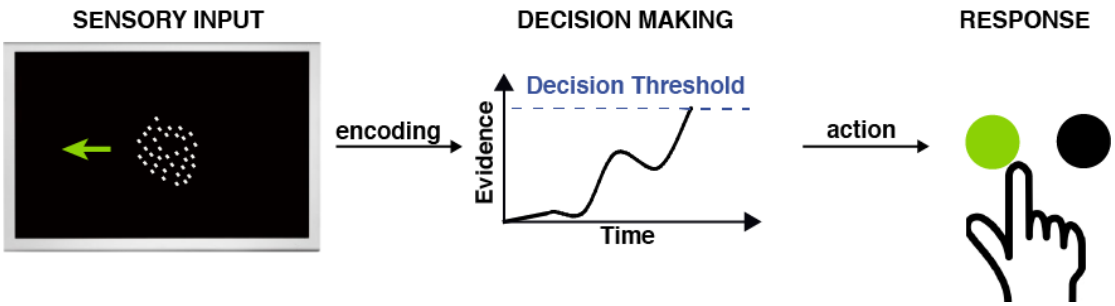

Figure 2. ***Perceptual Decision Making.***
Decision making is usually assumed to be based on the accumulation of sensory input over time until the evidence for one choice alternative reaches the decision threshold. Subsequently an action is elicited.

Perceptual decision making is the process of making decisions based on sensory information, i.e. visual, haptic, olfactory signals (Newsome et al, 1989; Romo and Salinas, 2001; Uchida et al., 2006; Figure 2). Perceptual decision making is usually conceptualized in terms of evidence integration over time (i.e. using the framework of sequential sampling models; Figure 2, middle). Fundamental findings have been made, by studying decision making using psychophysical motion discrimination tasks in binary forced choice settings (Figure 2A, left and right). For example, a participant has to discriminate between two directions of motion (left or right) of a random dot kinematogram (RDT) in a limited amount of time (up to one second) and indicate her decision by pressing a button (Figure 2, right). The random dot stimulus consists of a set of moving dots – visible in a circular area on a screen- out of one fraction of dots move coherently into the same direction and others move randomly about (Newsome et al., 1989). This paradigm lends itself most suitably to the study of decision making since the neural basis of motion perception is in this case properly understood (Maunsell and Newsome, 1987; Zeki et al., 1991; Logothetis et al., 1994; Tootel et al. 1995b; Bair et al., 2002).

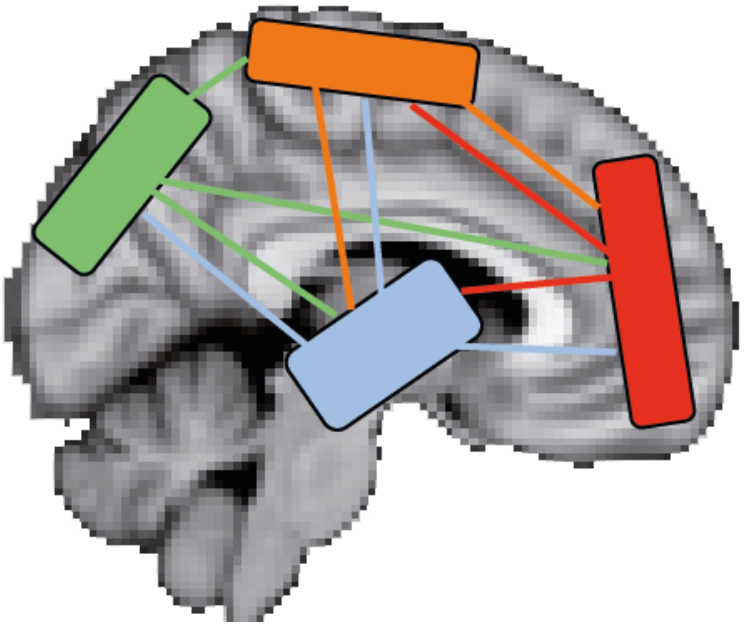

Figure 3. ***The neural basis of perceptual decision making.***
Simplified illustration of the neural bases of perceptual decision making. It is assumed that different heterarchically interacting brain systems subserve decision making.

Research on perceptual decision making has so far uncovered certain mechanisms of decision making in animals and in humans and mapped them onto distinct brain systems. For instance, evidence accumulation and the formation of a decision variable has been mapped to prefrontal and parietal cortical structures in humans as well as planning of a motor response and its selection has been mapped to pre-motor and basal ganglia structures (cf. Gold and Shadlen, 2007; Heekeren et al. 2004; Ho et al., 2009; Philiastides et al., 2011; Hare et al., 2011b). It is assumed that perceptual decision making is based upon heterarchically interacting neural information processing stages that encompass multiple brain regions (Figure 3; Green and Heekeren, 2009; Philiastides and Heekeren, 2010).

3. Empirical evidence: Neurophysiology

Neurophysiological work in monkeys has provided the first empirical evidence observed in sensorimotor neurons (sensory and motor related information processing) that accumulate noisy sensory evidence in line with the

sequential sampling framework (cf. Romo and Salinas, 2001; Gold and Shadlen, 2001; Smith and Ratcliff, 2004; Gold and Shadlen, 2007). Single-unit recording studies in monkeys have provided evidence for a close link between choice behavior and the activity of neuronal populations in sensory regions, i.e. primary somatosensory cortex (SI) and visual area MT (Britten et al., 1996; Romo et al., 2002). In those studies a decision problem is often framed as a simple binary choice difficulty. A monkey has to discriminate the direction of motion in random-dot kinetograms with different degrees of motion coherence in one of two opposite directions (cf. Newsome et al., 1989). In other cases a monkey has to compare tactile frequency differentiation stimuli (cf. Romo et al., 2004). The response is usually given via a saccade or a button press to indicate a decision. Neural activity profiles of sensory neurons in downstream processing areas such as the lateral intraparietal area (LIP) and the frontal eye field (FEF) reflect a process analogous to the accumulation of evidence (Britten, et al., 1996; Shadlen and Newsome, 1996; Gold and Shadlen, 2007). In these studies, electrophysiological recordings show that neurons in the macaque LIP increase and sustain firing rates up to the moment of a decision and the subsequent action (i.e. a saccade towards a target) (Shadlen and Newsome, 2001; Kiani, et al., 2006). Based on this research it has been proposed that sensory evidence supporting choice alternatives (here the two directions of motion) is integrated in a way comparable to a statistical likelihood ratio test (Gold and Shadlen, 2007). This claim has been subsequently supported by several quantitative computational modeling approaches with varying levels of neural and psychological detail of decomposition (cf. Lo and Wang, 2006; Bogacz et al., 2006; Deco et al., 2012).

Romo and colleagues (Romo et al., 2002) discovered similar patterns of activity for tactile discrimination tasks in neurons located in the somatosensory cortex and ventral premotor cortex (PMv, Romo et al., 2004). They recorded neural activity from single neurons in primary somatosensory cortex (SI) while monkeys performed a vibrotactile discrimination task, in which they had to decide which of two sequentially presented flutter stimuli

had a higher frequency. Trial-to-trial fluctuations in the firing rate of SI neurons predicted the monkeys' choices, and the average firing rate of SI neurons increased monotonically with increasing stimulus frequency pointing again towards the evidence accumulation framework.

All of the above mentioned studies included parametric variations of controllable task parameters – such as variations of stimulus or response difficulty, for example by changing the stimulus coherence (frequency in the vibrotactile task, motion coherence in the random dot stimulus), or by varying the allowed time for deliberation. This approach results in a tight link between neural activity, task conditions and decision making behavior. In addition, the same experimental manipulations enable us to understand that during a perceptual decision, different sources of information are combined and used by the decision maker to adjust to changing circumstances in an adaptive way.

Finally, electrical microstimulation studies provided causal evidence for a close link between neural activity and decision behavior in both the somatosensory and the visual domain (Romo et al., 1998; Ditterich et al., 2003). For instance, when the vibrotactile stimuli were replaced with analogous direct electrical microstimulation of primary somatosensory cortical neurons, the monkeys showed a very similar decision making pattern as under normal experimental conditions (Romo et al., 1998). Similarly, electrical microstimulation of directionally selective neurons in area MT caused the monkey to choose the neurons' preferred direction more often: when neurons tuned to rightward motion were stimulated, the monkey was more likely to make an eye movement to the target on the right (Ditterich et al., 2003; Hanks et al., 2006). Microstimulation of these neurons also quickened the decision in favor of the preferred direction and slowed the decision in the opposite direction (Ditterich et al., 2003). Thus, in both instances, the visual and the somatosensory domain, microstimulation has provided direct causal evidence for a tight link between the representation of sensory evidence in sensory regions, an activity-related threshold mechanism and perceptual decisions. In summary, these neurophysiological findings in the monkey support the basic

hypothesis of evidence accumulation up to a boundary for decision making in the brain.

An important concept that has emerged from modeling neurophysiological data of monkey experiments is that perceptual decisions are made, at least in part, by integrating over the sensory evidence represented by sensory neurons in order to form a decision variable (Gold and Shadlen, 2007). Neuronal activity in areas involved in decision-making gradually increases and then remains elevated at a stable level until an action is implemented (which determines the decision process). Notably, although the rate of increase in neural activity is slower during more difficult trials than during easier trials, the final level of activity is comparably pointing to a generalizable threshold mechanism (Roitman and Shadlen, 2002).

During the vibrotactile frequency-discrimination task described earlier (cf. Romo et al., 2003), neuronal populations in the monkey brain that are downstream from the primary and secondary sensory areas, such as the prefrontal, medial premotor and ventral premotor cortices, form a decision variable. This is done by respectively computing the difference in the activities of populations of sensory neurons in the secondary somatosensory cortex (SII) that prefer high and low frequencies (Romo et al., 2003; de Lafuente and Romo, 2005, Hernandez et al., 2002, Romo et al., 2004). Equally, during the direction-of-motion visual discrimination task, cells in regions downstream from area MT, such as LIP, FEF, and the dorsolateral prefrontal cortex (DLPFC), form a decision by computing the difference in the activities of neural populations from area MT that code for opposite directions of motion (Kim and Shadlen, 1999). Thus, in both sensory domains an integration by comparison operation that is bounded by a decision threshold appears to explain decision making. Together these findings indicate that brain areas such as frontal cortical as well as sensorimotor areas such as LIP and FEF integrate sensory evidence on which subsequent actions (saccades, arm movements, button presses) are based. It is noteworthy that regions in the monkey brain that have been implicated both in representing decision variables and in performing the comparator operation —LIP, FEF, DLPFC—

are at the same time areas that participate in selection, planning, and execution of motor responses. As such, when monkeys must choose in which direction a random-dot motion stimulus moves and indicate their decision with an eye movement, decision-related as well as saccade-related activity can be found in the FEF (Gold and Shadlen, 2003). Similarly, when monkeys perform the vibrotactile discrimination task, activity in medial and ventral premotor cortex reflects the temporal evolution not only of the decision-making process but also of action selection (Hernandez et al., 2002; Romo et al., 2004). Other neurophysiological studies have revealed that decision variables are represented in the superior colliculus, a midbrain region involved in the generation of saccadic eye movements (Gold and Shadlen, 2003; Horwitz et al., 2004). So far, both the predictions by the sequential sampling framework (i.e. accumulation of evidence over time), as well as the neurophysiological studies in monkeys, strongly suggest that the brain implements abstract and generalizable choice selection and action planning mechanisms.

3.1 Generalizability of the evidence accumulation framework for decision making

It should be noted that in many of the monkey studies, the monkeys were trained to indicate their final choice with a particular action. As the process of evidence accumulation is closely linked to the planning and implementation of an appropriate action, the monkeys could treat the decision problem as a motor problem. Therefore a common critique concerns the generalizability of the suggested information processing mechanisms and their mapping onto neural systems. It could be that the motor system is linked to perceptual decision making, simply because the decision problem can be formulated as a problem of which action to elicit (e.g. left- or rightward saccades). However, recent neuroimaging research has implicated comparable human brain regions into decision making. For instance, the supplementary motor cortex in humans has been found to play a role in modulating the decision boundary (Forstmann et al., 2008; Wenzlaff et al, 2011). Moreover, subcortical structures that are involved in action selection and motor control such as the

STN and the striatum have been implicated in decision making (Redgrave et al., 1999; Frank et al., 2007; Fleming et al., 2010). In addition, it has recently been shown that the STN is involved in decision threshold modulation (Cavanagh et al., 2011). It is assumed that the STN computes decision conflict and sends a signal to slow down action execution under high conflict (Frank et al, 2006, 2007). In line with this proposal, it was shown that the STN exhibits specific context dependent activity: STN activity is closely related to decision difficulty, reflected by modulated interaction with the inferior frontal cortex (IFC) under difficult choice settings (Fleming et al, 2010). Moreover, Frank and colleagues have shown that DBS of the STN leads to more impulsive (faster and less accurate) decisions when comparing high conflict choices (Frank et al., 2007).

4. Empirical Evidence: Neuroimaging

The general mechanism of evidence accumulation up to decision boundary or threshold that has emerged from the neurophysiological work in monkeys is also present in the human brain. Human neuroimaging studies have shown that accumulated noisy sensory evidence is integrated into a decision variable (an entity reflecting the difference in evidence for the choice alternatives, cf. Heekeren et al., 2004; Gold and Shadlen, 2007). Accumulated sensory evidence as well as action selection are encoded in overlapping and interacting neuronal populations throughout cortical and subcortical brain areas encompassing the basal ganglia (e.g. Forstmann et al., 2008; Ding and Gold, 2010), the parietal (e.g. Wong and Huk, 2008), premotor and motor (e.g. Forstmann et al., 2008; Donner et al., 2009; Wenzlaff et al., 2011) and frontal cortices (e.g. Heekeren et al., 2004, 2006; Philiastides et al., 2011). Together these findings strongly suggest that the latent neural information process supporting decision making can be adequately described by sequential sampling of sensory information, by which perceptual decision making can be understood as an integration of sensory information over time for each choice alternative up to a decision boundary. The information processing advantage

of this temporal integration means that noise inherent in sensory signals as well as in neural systems (i.e. transduction) is averaged out thus improving the signal-to-noise ratio. Note that this is very effective when noise is temporally uncorrelated (i.e. white noise).

Crucially, the disruption of neural activity supporting these mechanisms by means of neurostimulation e.g. DBS or transcranial magnetic stimulation (TMS) directly translates into changes of information processing and results in altered decision behavior (Frank et al., 2007; Philiastides et al., 2011; Cavanagh et al., 2011).

It is nowadays widely assumed that the concepts of evidence accumulation and decision thresholds represent aspects of general system level mechanisms of brain function that have been conserved during brain evolution (cf. Redgrave et al., 1999; Heekeren et al., 2008). One of the first neuroimaging studies for showing that the idea of evidence accumulation holds also for empirical data from the human brain used a simple perceptual categorization task in which human participants had to decide whether a picture that was presented to them was a house or a face. Notably, neural activity as measured by fMRI showed that activity in the left DLPFC covaries with the difference in evidence for face and house signals (Heekeren et al., 2004, 2006). The temporal evolution of neuronal activity during a similar perceptual categorization task supports once more the evidence accumulation framework (Philiastides et al., 2006a). Similar to the studies in monkeys, neural representations of sensory evidence can also be measured (i.e. for the Face in the Fusiform Face Area (FFA) and for the house in the Parahippocampal Place Area (PPA) using fMRI (Heekeren et al., 2004, 2006; cf. Philiastides et al., 2010)).

Single-unit recordings in monkeys have shown that neuronal activity in areas involved in decision making gradually increases and then remains elevated until a response is made. Importantly, these studies have shown that downstream cortical regions (i.e., further along the processing chain), such as LIP and the DLPFC, could form a decision by comparing the output of pools of selectively tuned sensory neurons up to a decision threshold and linking them

subsequently to actions. To test whether these results from neurophysiological research reveal basic principles that hold for the human domain, Heekeren et al. (Heekeren et al., 2006) asked human observers to make direction-of-motion judgments about dynamic random-dot-motion stimuli and indicate their choices with an eye movement-to one of two visual targets. In each individual, the authors localized regions that are part of the oculomotor network, namely the FEF and an eye-movement-related region in the intraparietal sulcus (IPS) that presumably corresponds to the LIP of monkeys (Sereno et al. 2001). During the period of decision formation (between the onset of visual motion and the cue to respond), the percent signal change of the blood oxygen level dependent (BOLD) signal in both the FEF and the IPS was highly correlated with the strength of the motion signal in the stimuli (Heekeren et al, 2006). These data are thus consistent with the single-unit studies in monkeys that reported that the FEF and the LIP participate in the process of forming a perceptual decision. More recently, Heekeren et al. investigated whether decisions might be transformed into motor actions in the human brain independently of motor planning and execution — that is, at an abstract level (Heekeren et al., 2006). Individuals performed the direction-of-motion discrimination task and responded with either button presses or saccadic eye movements. Areas that represent decision variables at a more abstract level should have shown a greater response to high coherence (easy) relative to low coherence (difficult) trials, independently of the motor system that is used to express the decision. Heekeren et al. found four such areas: the left posterior DLPFC, the left posterior cingulate cortex, the left IPS and the left fusiform / parahippocampal gyrus. Most importantly, the increase in BOLD activity in these regions was independent of the motor system that participants used to express their decision. The results from this fMRI study are in line with the finding by Kim and Shadlen that, in monkeys, neural activity increases proportionally with the strength of the motion signal in the stimulus (Kim and Shadlen, 1999). However, the findings in humans suggest that the posterior DLPFC is an important component of a network that not only accumulates sensory

evidence up to decision boundary to compute a decision but also translates this evidence into an action independently of response modality. Notably to date, neurophysiological studies in monkeys have not found neurons with an activity that reflects decisions independently of response modality. In fact, one could conclude from the neurophysiological studies in monkeys "to see and decide is, in effect, to plan a motor-response" (Rorie and Newsome, 2005). By contrast, in humans, various studies found regions of the cortex that responded independently of the motor effectors used. For instance, it was shown using multivariate fMRI analysis on a motion discrimination task with decoupled response modalities that perceptual decisions are independently encoded (from motor intentions) in visual and parietal regions of the human brain (Hebart et al., 2012). Moreover, a domain general signal of a decision variable has been recently discovered in the human brain (O'Connell et al., 2012). In that study participants observed a continuously presented annulus of which the contrast dropped at random intervals. Using electroencephalogram (EEG) analysis, it was shown that a decision variable is represented by a centro-parietal positivity (CPP) signal, which exhibits the characteristics of a decision variable: it is modality independent and also tracks decision formation that is independent from an overt motor response. Furthermore it has been shown in neuroimaging studies that decision related activity in the IPS performs evidence integration from visual motion area MT+ (Kayser et al., 2010a). Moreover, this mechanism can be influenced by other important factors such as attention (Kayser et al., 2010b). Finally, there is also causal evidence supporting the evidence integration framework. One particularly noteworthy study shows that TMS of the DLPFC - the region, which has been previously assumed to compute the decision variable (the integration of accumulated evidence for the choice alternatives) but not the decision threshold – in combination with diffusion modeling - degrades the evidence accumulation process (Philiastides et al., 2011).

In conclusion, neurophysiological and neuroimaging results support the assumption that evidence accumulation models capture important aspects of

the latent information processing supporting simple perceptual decision making.

5. Perceptual decision making as sequential sampling.

So far, empirical evidence substantially supports the idea of perceptual decision making as the sequential accumulation of (noisy) sensory evidence over time up to a decision threshold for short timescales (hundreds of milliseconds).

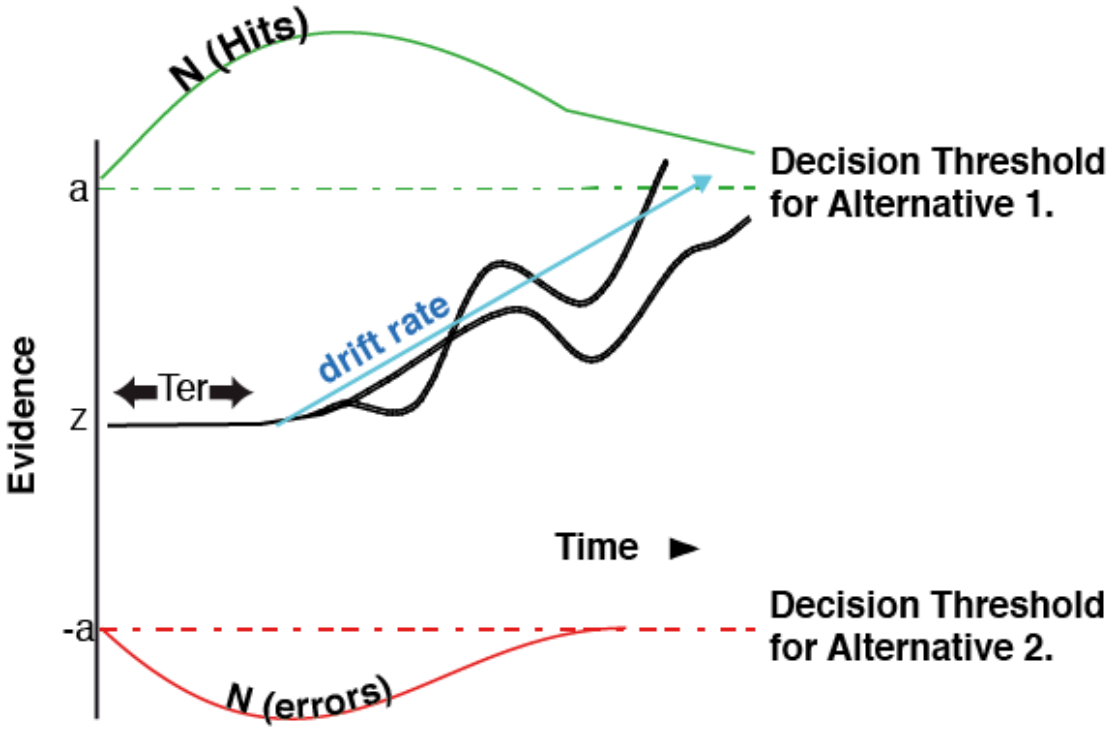

Figure 4. ***The Drift Diffusion model of a two-alternative forced choice task.***
*The DDM allows for a detailed analysis of decision processes by using different parameters such as the rate of information integration (**drift rate**), response (motor) preparation time and sensory transmission (**nondecision time, Ter**), bias/prior (**starting point, z**) or the amount of evidence needed for a decision (**threshold, a**). In general, the diffusion model assumes that noisy sensory evidence is sequentially integrated over time (drift) until sufficient information is accumulated to make a decision (crossing the threshold) and to elicit a response. The diffusion model describes full reaction time data distributions (reaction time and response accuracy) for hits (in green on top) and misses (in red on top).*

One very prominent instantiation of the sequential sampling framework is the DDM, which has been widely applied in psychology and neuroscience

(Ratcliff, 1978; Smith and Ratcliff, 2004; Ratcliff and McKoon, 2008, Figure 4). This model computationally formalizes a decision process in the following way: The difference in (sensory) evidence between choice alternatives is sampled continuously in time and drifts towards a decision boundary until it is reached. The DDM captures very well behavioral reaction time data (distributions of reaction time and accuracy) from psychological (Ratcliff and McKoon, 2008), neuroscientific (Basten et al, 2011; Philiastides et al, 2006) and neuroeconomic experiments (Krajbich et al., 2011, 2012) and has the following properties that lend themselves well for the investigation of the decision threshold:

1. The DDM can be mathematically derived from optimal statistical tests such as the sequential probability ratio test (SPRT; Gold and Shadlen, 2001; Bogacz et al., 2006; Bogacz and Gurney, 2007). An optimal test is one that minimizes the time needed to make a decision given a performance level. Thereby it also maximizes the reward rate (Bogacz et al., 2006; Gold and Shadlen, 2007). Interestingly, SPRT, which implements optimal (or maximal time efficient) hypothesis testing, can be mapped elegantly on cortico-basal ganglia circuits, assigning a special computational role to the STN during decision making (Figure 5, Bogacz and Gurney, 2007; Gold and Shadlen, 2007; Ditterich, 2010). Such a reverse engineering approach could help trying to establish a unified framework of decision making.

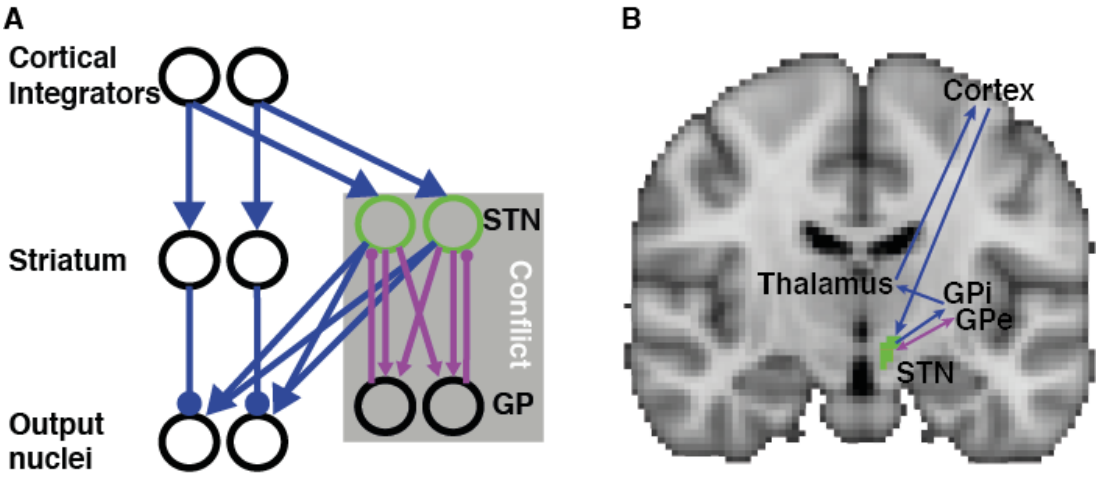

Figure 5.***The SPRT theory of optimal decision making and it's mapping on the hyperdirect pathway.***

(A) A simplified schematic of the neurocomputational model of cortico-basal ganglia network for optimal decision making (Bogacz and Gurney, 2007). The STN receives direct signals from cortical integrators and together with the globus pallidus (GP) computes decision conflict in order to send a „hold-your-horses" signal (Frank et al. 2007) to basal ganglia output structures in order to adjust decision making. The circles denote neural populations, arrow lines, excitatory connections and circles at the end of lines inhibitory connections. Colors of the lines in (A) match the hyperdirect pathways schema in (B). (B) The hyperdirect cortico-basal ganglia pathway (Nambu et al., 2002). The hyperdirect pathway connects the cortex directly with the STN, bypassing the striatum (which usually is the entry point to the basal ganglia in the other two (direct and indirect cortico-basal ganglia pathways). The STN subsequently sends excitatory projections to the internal segment of the GP.

2. Biophysically inspired network models of great neural detail (implementing realistic neural dynamics and neural systems connectivity) instantiate a DDM like information processing mechanism. They optimally describe empirical results from neurophysiological decision making tasks, offer high biological realism (neural population dynamics, single cells dynamics and neural systems connectivity) and thus allow the formulation of testable system level hypotheses (Lo and Wang, 2006; Kiani et al., 2006).

3. Fundamental decision making phenomena, as observed in psychophysical tasks (i.e. forced choice tasks) such as the speed accuracy trade-off (SAT; Fitts, 1954; Wickelgren, 1977) can be readily explained using the diffusion model (Bogacz et al., 2006, 2010). The SAT describes the trade-off between

deliberation and response time. For instance, when a participant in a perceptual categorization task is instructed to respond accurately, this can be explained by longer evidence accumulation due to a higher decision boundary (Figure 6A, 6B). Moreover, it has been suggested that the brain uses this mechanism in order to maximize the reward rate (Figure 6C; Gold and Shadlen, 2002; Bogacz et al, 2006).

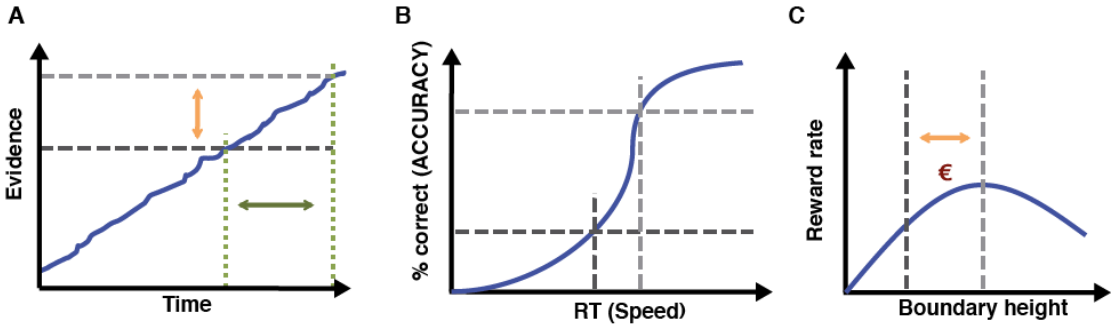

Figure 6. ***Decision threshold modulation, Speed Accuracy Trade-off and Reward Maximization.***

(A) Modulating the decision threshold allows for the trade-off between deliberation time and evidence accumulation. In case that circumstances require more accurate decisions, this in turn leads to a more extensive evidence accumulation and a higher decision boundary: since more noisy evidence is integrated over a longer period of time, which results in slower decision making. Faster decisions entail less extensive evidence accumulation using a lower decision boundary and are thus less accurate. (B) The SAT, in which decision time and error rate are negatively related, can be readily explained by a decision threshold mechanism (higher boundary → more evidence accumulation → slower reaction time and vice versa. (C) Threshold modulation enables reward maximization, as reward is a function of time and accuracy (cf. Gold and Shadlen, 2002).

It has been discovered that the variables and mechanisms of the sequential sampling framework that support decision making are of compelling biological relevance and can be mapped onto different features such as attention, or deliberation time (Heekeren et al., 2008; Philiastides and Heekeren, 2010; Kayser et al., 2010b). Nevertheless, evidence accumulation up to a threshold per se is insufficient to account for effective decision making. A decision also has to entail a mechanism that can flexibly adjust the decision criterion in order to balance decision-relevant factors such as for example sensory evidence, deliberation time, decision conflict, rewards, or values (Figure 6C;

Simen et al., 2006, Bogacz et al. 2006; Cavanagh et al., 2011; Krajbich and Rangel, 2011). Some theoretical knowledge about mechanisms of decision thresholds has been accumulated (Usher and McClelland, 2001; Simen et al., 2006; Lo and Wang, 2006; Bogacz et al., 2006; Diederich and Busemeyer, 2006; Simen, 2012). These formal conceptions suggest that modulation of the decision threshold is a general mechanism that is a) applicable to different variants of computational models, and b) is required for various cognitive processes, i.e. temporal duration estimation, memory retrieval, value comparison (cf. Kiani et al., 2006; Balci et al., 2011; Hanks et al., 2011). However, little is known about how and where in the brain decision thresholds are instantiated.

6. Research Aims

A particular important question thus concerns the neural mechanisms of decision thresholds, especially under the assumption that the decision threshold constitutes a general mechanism by which different choice relevant demands guide decision making. The fact that a decision threshold enables us to adjust our decisions and hence the adaptive interaction with the environment, constitutes the general motivation for this research project. Consider, for example, a reward based perspective (i.e. Ratcliff and Frank, 2012). Herein, understanding the mechanisms of the decision threshold is of particular interest, as the threshold is under the influence of the decision maker.

Previous research has shown that decision thresholds are influenced by distinct factors such as value, bias, conflict or reward in order to increase reward rate (cf. Gold and Shadlen, 2002; Chittka et al., 2009; Domenech and Dreher, 2010; Hare et al., 2011b; Cavanagh et al, 2011). Hence, one very straightforward approach is to use situations during which deliberation time and evidence accumulation (like in SATs, Figure 5B and 5C) are traded off in order to maximize rewards through a modulation of the decision threshold. This will allow a better understanding of the implementational as well as the algorithmic level of decision making (see Introduction, cf. Marr, 1983).

Equally important is the computational goal of the system. Here, neurocomputational models of optimal decision making and their mapping onto neural structures (Bogacz and Gurney, 2007) allow us to test specific computational goals that have been ascribed to particular structures, i.e. the proposal that the STN computes decision conflict and dynamically modulates the decision threshold (Frank, 2006; Bogacz and Gurney, 2007; Cavanagh et al., 2011).

To summarize, my dissertation focused on the following two research questions:

What is the neural representation of decision thresholds?

Do neurocomputational models of optimal decision making in cortico-basal ganglia networks reflect a neurally plausible mechanism for the regulation of decision processes?

In the following section I will describe in detail the two dissertation projects in which I tried to understand these questions.

7. Research studies

This section contains detailed summaries of two research projects. The first summary concerns the project on the neural mechanism of decision threshold modulation. The second summary elucidates the project on the neurocomputational accounts of optimal decision making.

7.1 Neural mechanisms of reward rate optimization in perceptual decision making.

Keywords: Reward Maximization, threshold modulation, fMRI, connectivity, diffusion model

Overview

Decision threshold modulation is a fundamental mechanism in higher brain function as it allows for the flexible adjustment of behavior (i.e. response initiation, value anticipation or memory retrieval) for instance under changing circumstances.

Decision makers determine (rewarded) perceptual decisions by collecting evidence until reaching a point of choice. They can either make decisions quickly, thereby risking more errors, or make decisions carefully, thereby risking to have fewer opportunities for being maximally rewarded, i.e. decision makers have to trade off speed and accuracy when they try to optimize reward. Single unit recording studies in monkeys as well as neuroimaging studies in humans have shown that cortical and striatal brain regions are involved in this SAT (Gold and Shadlen, 2002; Forstmann et al., 2008; Bogacz et al., 2010; Wenzlaff et al., 2011), although their interaction remains unclear. Computational network models suggest a modulation of connectivity (synaptic efficiency) between striatal and cortical neurons as the neurobiological mechanism by which decision makers adapt their behavior and thereby optimize their reward rate.

Theoretical Background

From a computational standpoint a modulation of the decision threshold can be accomplished either by adjusting the required amount of accumulated evidence or by changing deliberation time through the application of a time-dependent stopping rule (Busemeyer and Townsend, 1993; Gold and Shadlen, 2007). However, it is not established how an adjustable decision threshold for reward maximization is implemented in the brain.

Recent evidence suggests that decision threshold modulation is implemented in cortico-basal ganglia circuits (Lo and Wang, 2006; Forstmann et al., 2008; Cavanagh et al., 2011). A change in synaptic strength between connections within those networks has been proposed as a candidate neural mechanism supporting decision threshold modulation (Lo and Wang, 2006; Kiani et al., 2006). This proposal is based on the observation that activity in the basal ganglia generally increases until a neural activity bound is reached and motor execution is initiated. In this context, the most efficient way to speed up or slow down responses to accommodate better or worse stimulus quality is to modulate the synaptic strength between cortical neurons accumulating decision evidence and the basal-ganglia neurons that initiate motor execution when a neural activity bound is reached.

Hypotheses

Consistent with previous findings, we hypothesize that brain mechanisms for perceptual decision-making mechanisms adjust decision thresholds (to maximize reward) by modulating connectivity among brain regions that are involved in evidence accumulation, time processing, and action selection. These components are represented by the DLPFC, which accumulates the relative evidence for choice alternatives in perceptual decision-making tasks (Heekeren et al., 2004, 2008; Philiastides et al., 2011, Wenzlaff et al., 2011) and the cerebellum, which has been implicated in temporal processing (Ivry et al., 1988; Dreher and Grafman, 2002; Lewis and Miall, 2003; Ivry and Spencer, 2004; Grondin, 2008). These regions communicate with the striatum, the main input structure of the action selection system (Selemon and Goldman-Rakic, 1985; Graybiel et al., 1994; Middleton and Strick, 1994;

Hoshi et al., 2005). Using a multimodal approach we investigated whether decision threshold modulation for reward maximization is accompanied by changes in effective connectivity (here defined as psycho-physiological interactions; Friston et al., 1997) within cortico-striatal and cerebellar-striatal networks during the decision phase.

Our hypotheses follow from the aforementioned considerations:

1. *We expect people to adjust their decision making to different reward schedules in order to maximize rewards.*
2. *A threshold modulation version of the diffusion model should account for the RT data.*
3. *Neural mechanisms underlying threshold modulation for reward maximization can be revealed using a connectivity analysis of fMRI data, which estimates the effective connectivity between brain regions mediating decision making (specifically between DLPFC, striatum and cerebellum) during the decision phase.*

Methods

Task

22 subjects (11 females, mean age 28, +-3,7 years) were recruited from an in-house database at the Max Planck Institute for Human Development, Berlin. To investigate this connectivity hypothesis, participants performed a two alternative forced choice random motion dots task while their brain activity was scanned with fMRI at 3T. Participants performed the task repeatedly in blocks, in which rewards emphasized either accuracy, or speed, or both. Hence participants had to trade off speed and accuracy depending on the reward condition to obtain as much reward per block as possible. Assuming that participants' behavior is well described by a sequential sampling model of decision making, they could maximize their overall task reward by adjusting the amount of evidence required before making a decision.

Data analysis

Behavioral data were analyzed with a repeated measures analysis of variance (rmANOVA) to assess the effect of payoff conditions on decision making. Computational model parameters were estimated using the *Diffusion Model*

Analysis Toolbox (DMAT; Vandekerckhove and Tuerlinckx, 2008). We fitted the standard version (i.e., boundary modulation, nondecision time modulation, drift rate modulation, etc.) and an extended version (i.e. collapsing boundary, by courtesy of Jon Malmaud and Antonio Rangel) of the diffusion model to experimental data. The models' goodness-of-fit values were compared using the Bayesian information criterion, a model selection criterion that incorporates sample size, number of estimated parameters and a likelihood function for the estimated model (BIC; Schwarz, 1978). FMRI data were analyzed using a mixed effects general linear model (Mumford and Poldrack, 2007). FMRI data analysis was performed on the High-Performance Computing System Abacus (http://www.zedat.fu-berlin.de/Compute) at Freie Universität Berlin with FSL 4.1.2.

Results

Behavioral and modeling results indicate that human subjects modulated their decision threshold to maximize net reward. Neuroimaging results indicate that decision threshold modulation was achieved by adjusting effective connectivity within cortico-striatal and cerebellar-striatal brain systems; the former being responsible for processing of accumulated sensory evidence, and the latter being responsible for automatic, sub-second temporal processing. Participants who adjusted their threshold to a greater extent (and gained more net reward) also showed a greater modulation of effective connectivity. These results reveal a neural mechanism that underlies decision makers' abilities to adjust to changing circumstances in order to maximize reward. The results suggest that depending on the prevailing optimal strategy, reward optimization is achieved by way of modulating the coupling between cortical and striatal regions.

7.2 Deep brain stimulation reduces the influence of decision conflict in perceptual decision making.

Keywords: Deep Brain stimulation, Subthalamic nucleus, Optimization, Speed-Accuracy Trade-off, cortico-basal-ganglia circuit, neurocomputational models

Overview

Neurocomputational models based on the multihypothesis sequential probability ratio test (MSPRT) of the basal ganglia (Gurney et al., 2001; Bogacz, 2007; Bogacz and Gurney, 2007) have proposed that the STN plays a crucial role for threshold setting during decision making. The STN sends a breaking signal to the output structures of the basal ganglia effectively slowing down decision making when decision conflict exits (Frank, 2006). This has an effect on sensorimotor transformations in PD patients, as DBS of the STN impairs this conflict computation leading to more impulsive decision making during high conflict choices (Frank et al., 2007; Zaghloul et al., 2012).

Theoretical Background

Theoretical models by Bogacz and colleagues (Bogacz, 2007; Bogacz and Gurney, 2007) show how the cortico-basal ganglia network and the STN specifically can implement an optimal decision making procedure known as the MSPRT (Baum and Veeravalli, 1994). In this procedure, sensory evidence is accumulated only as long as it is necessary to gain a required level of confidence, and thus MSPRT is thought to minimize decision time for any specified level of accuracy. The MSPRT model predicts that disrupting information processing in the STN as for example with DBS should fundamentally change the way in which available sensory information is used to form simple decisions. More specifically, the computational models predict that DBS, which may disrupt information processing in the STN, should diminish the influence of task difficulty on reaction time (RT).

High frequency stimulation of the STN using DBS alleviates extrapyramidal side effects of PD patients. This stimulation elicits at the same time impulsive decision making under decision conflict. During high conflict choices, while under the influence of DBS, patients tend to respond rather quickly, not slowing down their decision making in order to account for the difficulty of the

decision (Frank et al., 2007; Wylie et al., 2010; Klostermann et al., 2010; Zaghloul et al., 2012). In particular Frank and colleagues (cf. Frank et al., 2007; Cavanagh et al., 2011) have shown that DBS elicits premature judgments under high conflict trials. In their studies, PD patients with DBS turned on are unable to appropriately adjust deliberation during high conflict decisions between two equally rewarding alternatives. Based on the findings that a) the STN encodes decision conflict during decision making (cf. Zaghloul et al., 2012) and b) influences the decision threshold (cf. Fleming et al., 2010; Cavanagh et al., 2011), we can probe neurocomputational models of optimal decision making that ascribe a central computational role to the STN for the modulation of the decision threshold. This will enhance our understanding on neural mechanisms of decision threshold.

Hypotheses

Based on the abovementioned empirical findings and theoretical considerations, we put forward following hypotheses:

1. *Response data from the DBS ON condition are better fit by a race model account.*
2. *Response data from the DBS OFF condition are better fit by a diffusion model account.*
3. *We expect main effects of DBS, coherence and SAT instruction on RT and accuracy.*
4. *We expect interactions of these factors, especially during high conflict, low coherence trials as STN computation is assumed to be crucial during the computation of high conflict decisions.*

Methods

Task

To test our predictions we asked PD patients to judge the direction of prevalent motion in RDTs under different DBS states. Patients were asked to perform a two alternative forced choice perceptual judgment task while their DB stimulator was respectively turned on or off. Trials differed in difficulty (motion coherence) and response instruction (fast or accurate). 10 young PD patients with implanted bilateral deep brain stimulators (DBS) (2 females, mean age, 57,3 +- 5,2 years) were recruited during their annual consultation meeting at Charité University Medicine Berlin, Department of Neurology, Campus Virchow, Berlin, Germany. All patients were on individually set, stable PD medication. The experimental session lasted approximately one hour (with short breaks) and began with a short control condition to acquaint the participants with the task. This was followed by the testing phase.

Data analysis

Data were analyzed in Matlab 2009b (The MathWorks Inc.) using a three way (DBS (ON, OFF) x SAT Instruction (FAST, ACCURATE) x Coherence (6 levels of motion coherence)) rmANOVA. Post hoc comparisons of the mean RT and response accuracy were computed by using paired sampled t-tests for low coherence, high conflict conditions (1.6% and 4.8 %) with correction for multiple comparisons.

Modeling of behavioral RT data was done in MATLAB (The MathWorks Inc.) using the optimization toolbox. We fitted pure race and pure diffusion models to data from each participant. Since we hypothesized that race and diffusion model fits would differ for reaction time data collected under different DBS states, we fitted each of the models separately to participant's behavior. Due to the small number of trials (i.e. 20) per condition (determined by combination of DBS state, SAT instruction and coherence) for each patient we decided not to compare the shapes of experimental RT distributions with distributions of the models, but instead we fitted the models to error rates (ER) and mean RT for each condition. This approach was further supported by the low variance (high noise) in RT for the different coherence levels (for more see discussion

section). Since each patient was tested in 12 conditions within a given DBS setting, ER and mean RT provide 24 data points constraining fits of each model. Due to limited data points (i.e. 24) to which we were fitting each model, we maximally constrained the race and diffusion models and fit them with as few parameters as possible, following the approach of Ditterich (2006). We ignore variability in parameters (drift, starting point, non decision time) present in the full diffusion model. Furthermore, instead of estimating separate drift parameter for each coherence condition, we follow the approach of Ditterich (2006).

Results

Behavioral results indicate that DBS significantly influences performance for difficult perceptual judgments as well as for the magnitude of adjustment between response instructions. In particular, when DBS is turned off, RTs increase substantially as the task becomes more difficult. By contrast, when DBS was turned on, the influence of task difficulty on RT was significantly lower. Notably, these findings are consistent with computational models, which suggest that the STN is crucial for adjusting decision making on difficult, high conflict trials. Individual data fits of evidence accumulation models demonstrate different information processing under distinct DBS states. Together these findings suggest a crucial role for the STN in adjusting decision making during high-conflict trials in perceptual decision making.

8. Discussion

This chapter contains a discussion of the two studies presented in the previous chapter. After a separate examination of each project, I will lead over to a conclusion, in which I will integrate the results of the two studies. Finally, I will consider how the findings can be used for future research and what questions can be raised.

Neural mechanism of threshold modulation

The first project presents the convergence of evidence encompassing behavioral data, neuroimaging data, and computational modeling results, which suggests that decision threshold modulation for reward maximization is instantiated through a change in connectivity within cortico-striatal and cerebellar-striatal functional brain circuits during the decision phase; the former being responsible for processing of accumulated sensory evidence and the latter being responsible for automatic, sub-second temporal processing. Our findings are consistent with previous empirical and theoretical accounts (Lo and Wang, 2006; Bogacz et al., 2006; Salinas, 2008; Forstmann et al. 2008; Deco et al., 2010; Cavanagh et al. 2011; Mansfield et al., 2011). Although our task bears some similarities with recent studies investigating neural correlates of the SAT (Forstmann et al., 2008; Forstmann et al., 2010; Bogacz et al., 2010; Wenzlaff et al., 2011; van Maanen et al. 2011), it is important to note crucial differences between those studies and the present study: SAT studies typically instruct participants to respond in a specific fashion (i.e. fast or accurate) in fairly easy perceptual categorization trials (for example 60 % motion coherence, as in Forstmann et al., 2008). In contrast, we manipulated participants' behavior by changing rewards and costs for hits and misses at an adaptively defined performance level (where stimulus coherence is low), i.e. participants had to use a combination of elapsed time and evidence when they made a decision to maximize net reward. Crucially, the task used in the present study has different biological implications and relevance compared to the standard SAT task design with explicit response instructions in two ways. First, an explicit instruction before the actual decision

leads to a fixed strategy set prior to the decision phase, which is not optimal when considering naturalistic choice circumstances with varying levels of sensory evidence or available time. Secondly, it will also lead to a different set of brain activities and thus models that can explain it: as it is assumed that the instruction will lead to a preactivation of brain systems encoding the responses. Previous SAT studies looked at changes in brain activity especially during the instruction phases, assuming a preactivation of brain areas to set the stage for deciding in a specific way. We specifically focused our analysis on the actual decision phase (encompassing stimulus presentation, decision making and responses) to understand, how accumulated evidence and elapsed time influence decision threshold modulation on-line. Our data support the view that decision threshold modulation for the maximization of reward is implemented as a change in connectivity within decision relevant brain systems. This is in line with recent studies showing that sensory as well as motor neurons change their activity and thus their interaction online when trading speed with accuracy (Heitz and Schall, 2012)

Neurocomputational models of optimal decision making

The second project combined psychophysical experimental methods and computational modeling to test an algorithmic theory of cortico-basal ganglia computation for optimal action selection (Bogacz and Gurney, 2007; Bogacz, 2007). It is important to note that this study extends previous empirical findings on STN computation for decision making (cf. Fleming et al., 2010; Mansfield et al., 2011; Zaghloul et al., 2012) to the domain of perceptual decision making while at the same time confirming computational models of decision making based on the MSPRT. It has been shown that MSPRT presents a framework for optimal decision making (Bogacz et al., 2006; Gold and Shadlen, 2007). This property of optimality has been analytically demonstrated for accuracy levels approaching 100% (Dragalin et al., 1999). In simulations with lower accuracy, MSPRT achieved faster or equal decision times compared to simpler procedures (McMillen and Holmes, 2006). Significantly, our modeling approach empirically tests this algorithmic

framework. Our modeling results, especially the estimated values of the decision threshold parameter, indicate that the integration of decision conflict into the decision process relies crucially on the STN. The individual data fits of evidence accumulation models demonstrate different information processing under distinct DBS states. This illustrates the importance of considering different models of information processing to compare different states, both in healthy and patient populations when using computational modeling of decision making.

9. Conclusion

Both projects shed light on mechanisms of the decision threshold. We have approached this mechanism from two different directions, the goal level and the implementational level of information processing. The suggested benefits of this bidirectional approach are the final combination of both on the algorithmic level, resulting in a deeper understanding of the phenomenon we are interested in.

The first project started out from an implementational level perspective on the decision threshold, i.e. the question what neural systems support threshold modulation inspired by a neural network model (Lo and Wang, 2006; Figure 7, lower part in yellow). The second project started out from the goal level in that we considered a procedural transparent algorithm with the goal of optimal decision making (Bogacz and Gurney, 2007; Figure 7, on top in green). We know from these studies that a change in connectivity between decision relevant brain regions modulates decision thresholds during simple forms of decision making (cf. Domenech and Dreher, 2010; Green et al., 2012). Further, we have shown that optimal decision making algorithms capture important aspects of decision relevant computations in the STN (cf. Cavanagh et al. 2011). Together both approaches result in a better understanding, especially of the representations and neural information processes of the decision threshold and fill the conceptual gap between algorithms and their neural equivalents (see Figure 7; Heitz and Schall, 2012).

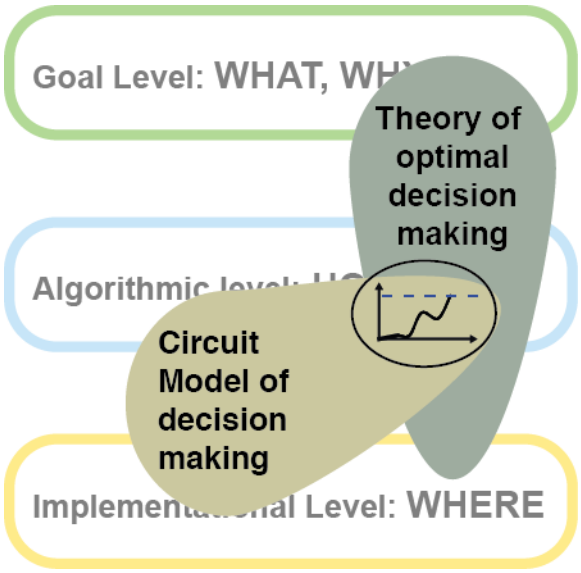

Figure 7. ***Combination of both research projects on Marr's three levels.***
The MSPRT account of optimal decision making starts from the goal level, particularly targeting optimal decision making. The threshold modulation study, insipred by a biophysical modeling account of neurophysiological data starts at the implementational level. Both approaches enhance our understanding of mechanims of the decision threshold, especially on the algorithmic level.

10. Future Research

In the last section of this dissertation I will discuss the potential implications of our research and future directions. Primarily, both studies show that we have to consider different model variants and types when comparing decision states.

Whereas the first study was based on hypotheses derived from a neural network model, we could only partly reproduce its predictions. By integrating time processing next to evidence accumulation, we explained our results and added a potential feature for future models of simple forms of decision making. In the second study, we showed that different types of sequential sampling models explain different DBS states. These states are related to STN functioning. This could be potentially relevant to determine to which data, i.e. from patient populations or healthy subjects, a computational model can be applied and intelligibly interpreted (cf. Maia and Frank, 2011).

In conclusion, our findings on the neural mechanism of decision threshold modulation could be highly relevant for the computational approach to the

understanding of psychiatric disorders that are accompanied by impulsivity, inhibitory control or inflexibility: for example approach avoidance disorders like anxiety or disorders such as attention-deficit hyperactivity disorder (ADHD) and schizophrenia (e.g. Rangel et al., 2008; Thagard et al., 2008; Mulder et al., 2010; White et al., 2010; Montague et al, 2012). We currently undertake an investigation on the effects of acute stress on decision making, especially on decision threshold modulation. Based on models that have suggested an alternative formulation of the decision threshold, i.e. urgency gating (cf. Cisek et al., 2009) we will test different models comparing for example linear, logarithmic, or exponential collapse over time and put them in relation to different (biologically defined) levels of acute stress.

Open questions that I consider valuable in order to arrive at a complete account of the decision threshold are first the question on the invariance of decision threshold mechanisms across different modalities and tasks. In this context we have to consider known effects of slight changes, i.e. stimulus duration (Rüter et al., 2012), or model parameterization (Dutilh et al., 2010; van Ravenzwaaij et al., 2012; Ditterich, 2012) may all have severe effects on the observed results and their conclusions. Secondly, the temporal profile for the adjustable decision threshold has been only theoretically investigated (Simen et al., 2009). This aspect is potentially very important, in learning or temporal processing for instance (cf. Simen et al., 2011). Thirdly, one might ask under which naturalistic conditions are optimal strategies achievable (cf. Kacelnik et al., 2011). We know that human and animal choices tend to be suboptimal in complex naturalistic environments. How does this fit with current computational models (cf. Bogacz et al., 2010a; Newell and Lee, 2010)? A first step in addressing this question would be to see how current models could explain and predict more complex decision situations. An example for that would be the investigation of the decision threshold mechanism in approach-avoidance situations, in which both cognitive as well as emotional attributes influence decision making (cf. Busemeyer et al., 2002).

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Supplements

Eidesstattliche Erklärung

Hiermit erkläre ich an Eides statt,

- dass ich die vorliegende Arbeit selbständig und ohne erlaubte Hilfe verfasst habe,
- dass ich mich nicht bereits anderwärts um einen Doktorgrad beworben habe und keinen Doktorgrad in dem Promotionsfach Psychologie besitze und
- dass ich die zugrunde liegende Promotionsordnung vom 02.08.2008 kenne.

Berlin, den 10. Dezember 2012 Nikos Green

Research Articles

Research Project 1.

Nikos Green, Guido Biele, and Hauke R. Heekeren (2012). **Changes in Neural Connectivity Underlie Decision Threshold Modulation for Reward Maximization.** The Journal of Neuroscience, 32(43): 14942-14950; http://dx.doi.org/10.1523/JNEUROSCI.0573-12.2012

Behavioral/Systems/Cognitive

Changes in Neural Connectivity Underlie Decision Threshold Modulation for Reward Maximization

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Using neuroimaging in combination with computational modeling, this study shows that decision threshold modulation for reward maximization is accompanied by a change in effective connectivity within corticostriatal and cerebellar–striatal brain systems. Research on perceptual decision making suggests that people make decisions by accumulating sensory evidence until a decision threshold is crossed. This threshold can be adjusted to changing circumstances, to maximize rewards. Decision making thus requires effectively managing the amount of accumulated evidence versus the amount of available time. Importantly, the neural substrate of this decision threshold modulation is unknown. Participants performed a perceptual decision-making task in blocks with identical duration but different reward schedules. Behavioral and modeling results indicate that human subjects modulated their decision threshold to maximize net reward. Neuroimaging results indicate that decision threshold modulation was achieved by adjusting effective connectivity within corticostriatal and cerebellar–striatal brain systems, the former being responsible for processing of accumulated sensory evidence and the latter being responsible for automatic, subsecond temporal processing. Participants who adjusted their threshold to a greater extent (and gained more net reward) also showed a greater modulation of effective connectivity. These results reveal a neural mechanism that underlies decision makers' abilities to adjust to changing circumstances to maximize reward.

Introduction

When making everyday decisions, we oftentimes incur opportunity costs, spending time deliberating one judgment at the cost of having time to consider others (Chittka et al., 2009). To maximize returns in situations in which multiple decisions need to be made, decision makers have to adjust their decision criterion (Gold and Shadlen, 2002).

Research on perceptual decision making has provided considerable first steps into general mechanisms of decision making (Shadlen and Newsome, 2001; Romo et al., 2004; Philiastides et al., 2006; Gold and Shadlen, 2007; Heekeren et al., 2004, 2008). Underlying processes have been well described by sequential sampling models (Smith and Ratcliff, 2004). One distinctly successful instantiation of this computational framework, the drift diffusion model, provides a well-fitting description of mechanisms for simple decisions (Smith and Ratcliff, 2004; Bogacz et al. 2006; Ratcliff and McKoon, 2008). Decisions are formed by continuously accumulating the relative evidence for the choice alternatives over time until a response boundary is crossed. The distance of boundaries from the starting point of the accumulation process determines accuracy and speed of decisions. More accurate decisions require longer accumulation and are thus slower, because more noisy evidence has to be integrated.

From a computational standpoint, a modulation of the decision threshold can be accomplished by either adjusting the required amount of accumulated evidence or changing deliberation time through the application of a time-dependent stopping rule (Busemeyer and Townsend, 1993; Gold and Shadlen, 2002; Fig. 1*A*). However, it is not established how an adjustable decision threshold for reward maximization is implemented in the brain.

Recent evidence suggests that decision threshold modulation is implemented in the corticobasal ganglia network (Lo and Wang, 2006; Forstmann et al., 2010; Cavanagh et al., 2011). A change in synaptic strength within this network has been proposed as a candidate neural mechanism supporting decision threshold modulation. This proposal is based on the observation that activity in the basal ganglia generally increases until a neural activity bound is reached and motor execution is initiated. In this context, the most efficient way to speed up or slow down responses to accommodate better or worse stimulus quality is to modulate the synaptic strength between cortical neurons accumulating decision evidence and basal ganglia neurons that trigger motor execution when a neural activity bound is reached (see Materials and Methods).

Consistent with previous findings, we hypothesize that brain mechanisms for perceptual decision-making adjust decision

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The authors declare no competing financial interests.

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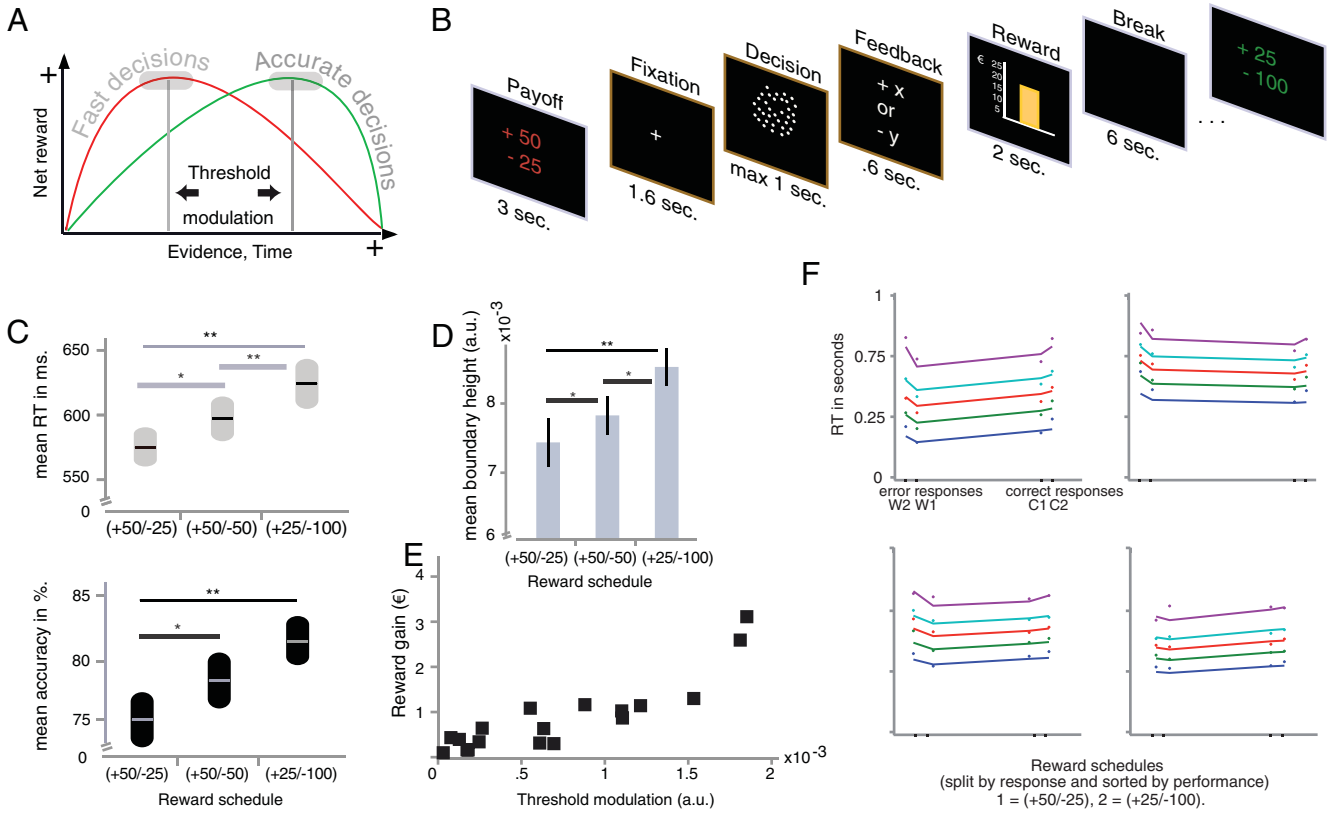

Figure 1. ***A***, Decision threshold modulation is reward maximizing under changing incentive structures (red and green lines). ***B***, Rewards and costs for hits and misses are presented at the beginning of each block of trials. Subjects receive per trial feedback and the projected reward in euros after each block. Overall time for the task is finite. Thus, response times influence the number of decisions that can be made. ***C***, Behavioral results. Top, Mean ± SEM RT: low-threshold state, 576.41 ± 17.48 ms; intermediate state, 597.04 ± 17.30 ms; high-threshold state, 624.07 ± 19.35 ms. Bottom, Mean ± SE of response accuracy: low-threshold state, 75.45 ± 2.13%; intermediate state, 78.45 ± 2.16%; high-threshold state, 81.62 ± 1.89% (percentage correct mean ± SEM RT and response accuracy differed significantly between threshold states, $*p < 0.05$, $**p < 0.001$, Bonferroni's adjusted). ***D***, Mean ± SEM group boundary parameter values for all threshold states from the best-fitting diffusion model: low-threshold state, 0.0739 ± 0.0035 a.u.; intermediate state, 0.0778 ± 0.0028 a.u.; high-threshold state, 0.0848 ± 0.0027 a.u. (boundary heights are significantly different between threshold states, $*p < 0.01$, $**p < 0.001$). ***E***, Magnitude of boundary modulation relates to reward. Reward gain is defined as the difference between projected reward with no threshold modulation and actual reward with boundary modulation. ***F***, Quantile probability plots of four randomly selected datasets.

thresholds (to maximize reward) by modulating connectivity among brain regions that are involved in evidence accumulation, time processing, and action selection. These components are represented by the dorsolateral prefrontal cortex (dlPFC), which accumulates the relative evidence for choice alternatives in perceptual decision-making tasks (Heekeren et al., 2004, 2008; Philiastides et al., 2011; Wenzlaff et al., 2011), and the cerebellum, which has been implicated in subsecond temporal processing (Ivry and Keele, 1989; Dreher and Grafman, 2002; Lewis and Miall, 2003; Ivry and Spencer, 2004; Grondin, 2008). These regions communicate with the striatum, the main input structure of the action-selection system (Selemon and Goldman-Rakic, 1985; Graybiel et al., 1994; Middleton and Strick, 1994). Using a multimethod approach, we show that decision threshold modulation for reward maximization is accompanied by changes in effective connectivity [psycho-physiological interactions (PPIs); see Materials and Methods] within corticostriatal and cerebellar–striatal networks.

Materials and Methods

Participants. Twenty-two subjects (11 females; mean age, 28 ± 3.7 years) were recruited from an in-house database at the Max Planck Institute for Human Development (Berlin, Germany). All subjects had normal or corrected-to-normal vision, were free of neurological and psychiatric history, and were briefed on the nature of methods used. All participants gave informed consent to participate according to the protocol approved by the local ethics committee. Complete datasets of 18 subjects were included in the full analysis, because two participants dropped out during experimental testing and two other participants had severe head motion during scanning (for details, see below).

Task setup. Subjects had to decide on the direction of motion (binary choice: left or right) of a dynamic random-dot stimulus and indicate their choice with a button press. Dots were white on a black background and were drawn in a circular aperture (~5° diameter) for the duration of one video frame (60 Hz). Dots were redrawn after ~50 ms at either a random location or a neighboring spatial location to induce apparent motion. The resultant motion effect appeared to move between 3°/s and 7°/s, and dots were drawn at a density of 16.7 dots per degree per second. The task was implemented with Presentation (version 0.70; Neurobehavioral Systems), the Psychtoolbox3 (www.Psychtoolbox.org), and an adapted version of the Variable Coherence Random Dot Motion Code Collection (www.shadlen.org/Code/VCRDM). Stimuli were displayed using VisuaStim goggles (Magnetic Resonance Technologies), consisting of two small thin-film transistor monitors placed directly in front of the eyes, simulating a distance to a normal computer screen of 100 cm with a resolution of 1024 × 768 pixels and a refresh rate of 60 Hz. Participants used VisuaStim Response Pads (Magnetic Resonance Technologies) to make their response by pressing a button with either their left or right thumb.

The task was partitioned into blocks using three alternating reward schedules: (1) +50/−25; (2) +50/−50; and (3) +25/−100 (Fig. 1*B*). These number pairs consist of gained points for a correct answer (left number) and lost points for an incorrect answer or a failure to respond

(right number). Blocks in all conditions were maximally 32 s long. These 32 s were filled with as many trials as possible. For example, if a participant would respond with an average reaction time (RT) of 600 ms per trial during a block, she would be able to complete 11 trials [32s/(0.6 s decision + 1.6 s fixation + 0.6 s feedback) = 11.4]. Within a block, a new trial was only issued if there was enough remaining time for a complete maximum trial [length of 3.2 s = fixation cross (1.6 s) + maximum stimulus presentation time (1 s) + feedback (0.6 s)].

Participants did not receive explicit response instructions but were informed that there is limited overall time for making decisions. Maximizing net reward under different reward schedules thus required adapting decision thresholds. For instance, when gains for correct responses were small and losses for incorrect responses were large, it was reward maximizing to avoid large losses by collecting more evidence and thereby increase the probability to respond accurately. Conversely, when gains were moderate and losses small, it was reward maximizing to respond faster (albeit on average less accurately) because as a result more decisions could be made during the experiment and in this way net reward increased. Hence, subjects were required to modulate their decision behavior by using either a lower threshold (leading to faster but less accurate responses) or a higher threshold (leading to slower yet more accurate responses) to maximize net reward in finite time (Fig. 1*A*). Performance was rewarded with up to €25.

Blocks were presented randomized, whereby the reward schedule for each block was shown once at the beginning of each block, displayed to the subject for 3 s. The decision phase immediately followed in blocks of trials (amount of total responses depended on participant's individual response speed). In each trial, subjects saw a fixation cross (1.6 s) after which the stimulus was presented. The stimulus was extinguished by a response or after 1 s, followed by feedback of 0.6 s. At the end of each block, participants were shown their current projected reward in euros (2 s) for the entire experiment: Reward (in €) = (€25/Total Score) × $\text{Score}_{\text{Reward Schedule}}$, where Score = $\text{Actual\_Score}_{\text{projected}}$ + $\text{Additional\_Score}_{\text{projected}}$. Using the 75% accuracy level as base-level performance (set by an adaptive staircase procedure; see below) for the speed condition, we calculated how much the subjects could earn (whereby the fastest included RT had to be >249 ms and RTs <250 ms were assumed to be fast guesses). Including the points per reward schedule, we computed a metric for rewards for the entire experiment with the aforementioned RT constraint. Subject's scores (which were determined by accuracy and response times) were then compared with this metric, and they were rewarded based on their score.

Participants received a 20 min practice immediately before they entered the scanner. During practice, subjects performed direction-of-motion discriminations for varying coherence levels and received per trial feedback on accuracy. Participants did not practice under the influence of reward schedules or response instructions. The subsequent scanning session totaled 1 h. While subjects were lying in the scanner but before any scanning protocol, an adaptive staircase procedure was used to determine an individual stimulus coherence level at 75% performance accuracy (Leek, 2001). This allowed us to obtain enough error responses for a good fit of the diffusion model to RT data (Ratcliff and Tuerlinckx, 2002; Vandekerckhove and Tuerlinckx, 2007). Moreover, a constant-coherence level allowed us to exclude effects of stimulus difficulty on decision threshold adaptation (Vandekerckhove and Tuerlinckx, 2007; Ratcliff and McKoon, 2008). The coherence level at which participants achieved 75% accuracy was low (group mean, 12%). We were thus able to minimize differences in attention between reward schedule conditions. It is assumed that low-coherence stimuli demand comparable focus on the task during all task conditions. Participants were debriefed with a questionnaire and a personal interview.

Behavioral data were analyzed with a repeated-measures ANOVA. For each individual dataset, all trials with RTs > = 2 SD from the mean were excluded from all analyses. Computational model parameters such as boundary height or drift rate were estimated using the Diffusion Model Analysis Toolbox (DMAT; Vandekerckhove and Tuerlinckx, 2008). We fitted the standard version of the model with constant decision boundaries and an extended version (including a collapsing boundary; courtesy of Jonathan Malmaud and Antonio Rangel, California Institute of Technology, Pasadena, CA) of the diffusion model to experimental data. The goodness of fit of the models values were compared using the Bayesian information criterion (BIC; Schwarz, 1978).

Neuroimaging. Subjects were scanned in a whole-body 3T Siemens TRIO MR system by acquiring 46 axial slices (216 mm field of view; 72 × 72 acquisition matrix; in-plane voxel dimensions, 3 × 3 mm; repetition time of 2500 ms; echo time of 29 ms; 80° flip angle) parallel to the anterior commissure–posterior commissure plane and covering the whole brain. Slice gaps were interpolated to generate output data with a spatial resolution of 3 × 3 × 3 mm. High-resolution T1 images (repetition time of 1900 ms; echo time of 2.52 ms; 9° flip angle; 192 sagittal slices; voxel size, 1 × 1 × 1 mm) were acquired, as well as field inhomogeneity measures and a structural fluid-attenuated inversion recovery image.

fMRI data analysis was performed on the High-Performance Computing System Abacus (http://www.zedat.fu-berlin.de/Compute) at Free University of Berlin with FSL [for FMRIB (Functional MRI of the Brain, Oxford, UK) Software Library] version 4.1.2, the open software toolbox from FMRIB (http://www.fmrib.ox.ac.uk/fsl/), and in-house developed MATLAB scripts (R2007a; www.mathworks.de). Regressors were convolved using a double-gamma hemodynamic response function. Motion parameters were checked for outliers [two participants with relative head movement greater than one voxel size (3 mm) were removed from the analysis] and added as regressors to the design matrix to reduce motion-related artifacts. Functional volumes were slice-time and motion corrected and spatially smoothed by using a Gaussian kernel of 6 mm full-width at half-maximum and high-pass filtered with $\sigma = 80$ s (2.5 times the maximum block length). Images were registered using linear transformations [FLIRT (for FMRIB Linear Image Restoration Tool); Jenkinson et al., 2002] with 7 degrees of freedom (d.o.f.) for individual functional (EPI) space to T1 and with 12 d.o.f. for T1 to standard space. For group-level results, individual-level contrasts were averaged using FLAME (for the FMRIB Local Analysis of Mixed Effects) 1 and 2 (including automatic deweighting of outliers) module in FSL (Beckmann et al., 2003; Woolrich et al., 2004), and one-sample *t* tests were performed at each voxel for each contrast of interest. Significant clusters on a familywise-error-corrected level of $\alpha = 0.05$ were identified with the threshold-free cluster enhancement (TFCE) algorithm implemented in the FSL program *randomize* (Smith and Nichols, 2009). From group-level activation maps of the decision phase, we calculated a conjunction map based on the initial general linear model decision phase group activation maps using a logical AND conjunction at a $p = 0.05$ corrected TFCE threshold (Fig. 2*A*). This conjunction map includes brain regions that show a significant increase in blood oxygenation level-dependent (BOLD) activity during the decision phase in all reward schedules. Considering our hypothesis that threshold adjustments are instantiated by changes in interaction between those brain regions mediating decision making, we selected regions of interest (ROIs) that are involved in representation and computation of the decision variables accumulated evidence (dlPFC) and available time (cerebellum) as seeds for a PPI analysis. To verify that the selected ROIs are functionally involved in the stipulated processes of evidence accumulation and available time processing, respectively, we compared parameter estimates for the decision phase under the different reward schedule conditions. Functional ROIs (Poldrack, 2007; Ramsey et al., 2010) were constrained by using a 50% anatomical probability threshold based on the anatomical probability atlases included in FSL [the Harvard–Oxford Subcortical Atlas (Caviness et al., 1996) for the dlPFC and the MNI Structural Brain Atlas (Diedrichsen et al., 2009) for the cerebellum]. ROIs were subsequently transformed from standard space into each individual's functional space using a linear transformation. Each individual ROI was checked to ensure that it is contained within the brain and within the anatomical ROI and was subsequently used to extract the time series of the seed regions for a PPI analysis (Friston et al., 1997). It is worth to consider in detail if changes in the strength of the cortico (cerebellar)-striatal synapses can be examined with fMRI by analyzing changes in effective connectivity with a PPI analysis. According to Friston and colleagues, a change in "effective connectivity" can be characterized as a change in the correlation of neural activity (and the dependent BOLD signal) between two neuronal

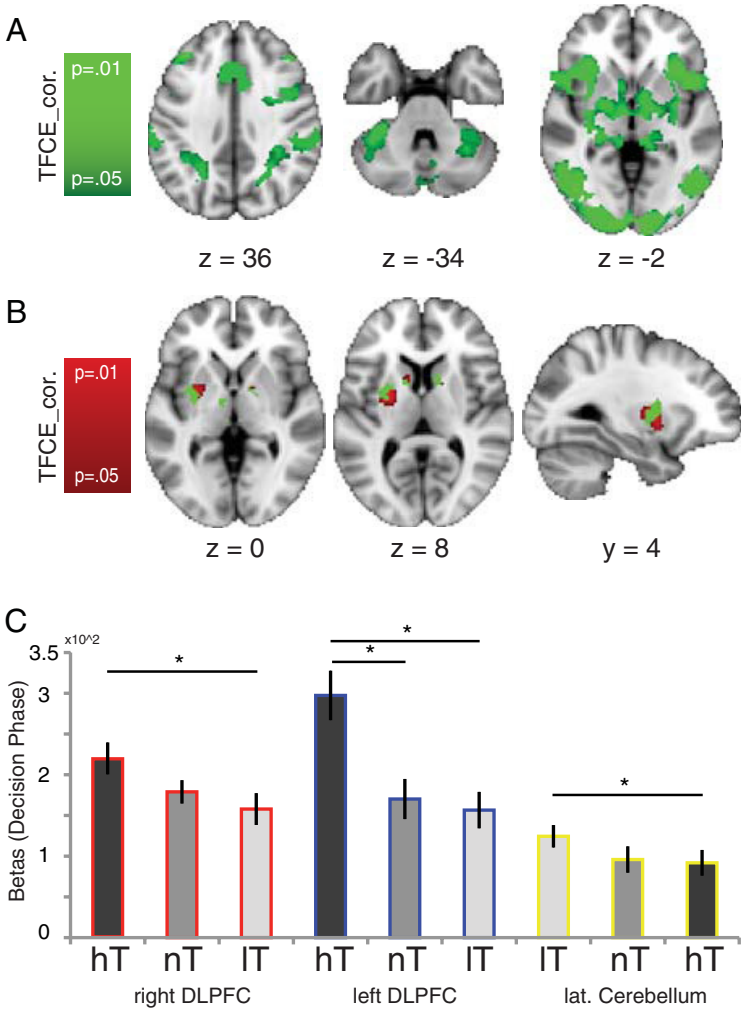

Figure 2. ***A***, Conjunction map of activated brain areas during the decision phase. ***B***, Threshold modulation covariation (red) overlap with decision phase activity (green). ***C***, Beta values of seed regions for low-threshold (lT), neutral-threshold (nT), and high-threshold (hT) states (red, right DLPFC; blue, left DLPFC; yellow, cerebellum); $*p < 0.01$.

populations from one state (or experimental condition) to another (Friston et al., 1993, 1997; Friston, 2011).

Significance testing of the results of PPIs for two dlPFC (left and right) and one cerebellar seed regions (left) was done in a predetermined basal ganglia mask (based on Harvard–Oxford Subcortical Atlas including bilateral caudate, putamen, nucleus accumbens, thalamus, pallidum, using no probability threshold), and correction for familywise error was achieved by applying small-volume correction. Next, to investigate whether voxels were correlated with boundary modulation, a whole-brain group analysis (high threshold > low threshold) with the additional covariate of the magnitude of boundary modulation (estimated with the diffusion model) was performed. Additional whole-brain PPI analyses were performed for the 10 most highly activated clusters during the decision phase (see Table 3).

Results

Participants made, on average, 815 decisions during the entire experiment. Training on the task before the scanning session and during the scanning session minimized error trials. On average, 2.1 responses (0.25%) were fast guesses (i.e., response time >250 ms) and participants did not respond within 1 s in 7.3 trials (0.85%).

Subjects altered their decision-making behavior to maximize reward by responding with decision threshold adjustments to reward schedules. They responded faster ($F_{(1.21,20.57)} = 17.361$, $p < 0.0001$) and less accurately ($F_{(1.722,29.28)} = 17.817$, $p < 0.0001$) during blocks of trials in which faster responses were reward maximizing compared with blocks in which slower, accurate judgments were more profitable (Fig. 1*C*). The number of completed trials differed significantly between the high-threshold condition (mean ± SD, 262 ± 6.8 trials) and low-threshold condition (mean ± SD, 277 ± 9.4; $t_{(17)} = 11.8$, $p < 0.001$) (mean ± SD, 276 ± 9.1 in the neutral-threshold condition). The number of completed trials indicates that participants adjusted their decision-making behavior to reward schedules; however, the examination of reward frequencies (number of accurate trials per condition) shows that this did not happen in an optimal manner: average ± SD reward frequencies were 207 ± 19 in the low-threshold, 215 ± 20 in the neutral-threshold, and 212 ± 19 in the low-threshold conditions. The differences high–low and neutral–low are statistically significant ($t_{(17)} = -2.3$, $p = 0.035$ and $t_{(17)} = -3.08$, $p = 0.006$, respectively), but high–neutral is not statistically significant ($t_{(17)} = -0.68$, $p = 0.49$). The lower reward frequency in the low-threshold condition is unexpected because, to optimize rewards, a larger number of completed trials should also lead to a larger number of accurate trials. The reduced reward frequency in the low-threshold condition suggests that participants on average responded too fast in this condition. That is, they implemented a lower than optimal decision threshold given their discrimination ability (as measured with the drift rate v of the diffusion model).

Subjects markedly adjusted their decision process by modulating their decision threshold, as indicated by model fits of the drift diffusion model to observed RT data (Fig. 1*F*). Model comparisons on different versions of the diffusion model indicated the modulating boundary version as the best-fitting model (lowest BIC score of 39,227 in the standard DMAT framework; see top part of Table 1). Additionally, we fitted an extended model that included an exponentially collapsing boundary parameter (also implemented in DMAT) to the RT data and compared it with the previously used versions. Model fits indicated the standard modulating boundary version as the best-fitting model (lowest BIC score of 25,620; see bottom part of Table 1). Moreover, subjects with a greater threshold modulation between high-threshold and low-threshold states gained more rewards (Fig. 1*E*). It is important to note that the interindividual differences in threshold modulation we observed are consistent with previous findings, which indicate that not all subjects adjust decision thresholds equally well (Bogacz et al., 2010).

Within each threshold condition, participants were more accurate in trials with faster RTs than in those with slower RTs. The main effect of response speed on accuracy was significant ($F_{(1,17)} = 46.14$, $p < 0.001$). These results are in line with the view that longer RTs between conditions (associated with increased accuracy) are caused by a different process than longer RTs within

Table 1. BIC model comparison on different standard (top) and extended (bottom) versions of the drift diffusion model

	BIC score (summed across individual subjects' model fits)
Standard diffusion model [free parameter(s) across reward schedules]	
No modulation across conditions	39, 354, Δ (current model − best model) = 77
Boundary	39,227 (best model)
Drift rate	39,458, $\Delta = 181$
Boundary and drift rate	39,623, $\Delta = 346$
Boundary and η (across-trial variability in drift rate)	39,603, $\Delta = 326$
Drift rate and η	39,629, $\Delta = 352$
Boundary and Ter (nondecision components of reaction time)	39,538, $\Delta = 311$
Extended diffusion model [free parameter(s) across reward schedules]	
Boundary	25,620 (best model)
Collapsing boundary	25,686, $\Delta = 66$
Drift rate and collapsing boundary	25,722, $\Delta = 102$
Ter (nondecision components) and collapsing boundary	25,731, $\Delta = 111$

Models were fitted to individual subjects' RT data. The model with a changing response boundary (across reward schedules) has the lowest BIC score of 39,227 for standard model and 25,620 for the extended model (summed individual model fits).

condition (associated with reduced accuracy). Within-condition slowing is likely to be a result of trial-to-trial variations in difficulty, in that participants slow down response in more difficult trials to maintain accuracy (although this has only limited success). This type of speed–accuracy tradeoff is described by the model of Lo and Wang (2006). In contrast, between-condition differences in RTs are not an adaptation to local variations in difficulty but an adaptation to the reward structure.

Corresponding to our hypothesis that threshold modulation is reflected in a change in effective connectivity between brain regions that process task-relevant decision variables and control action selection during the decision phase (Fig. 2*A*,*C*), we focused on ROIs that are involved in the representation and computation of accumulated evidence (dlPFC) and available time (cerebellum) and motor execution (basal ganglia). To verify the putative functional roles of those seed regions in the decision phase, we compared their respective parameter estimates for low-, neutral-, and high-threshold conditions (Fig. 2*C*). BOLD responses in both dlPFCs showed greater activation during the high(er)-threshold condition in which more evidence is accumulated compared with the low(er) evidence accumulation condition, in which faster responses are reward maximizing (Fig. 2*C*). For the cerebellar ROI, we observed the opposite pattern. Activation was greater in the low-threshold condition, which favors faster decision making compared with the high-threshold condition when slow(er) but on average more accurate decisions are reward maximizing. BOLD responses were greater in the cerebellum when deliberation time was of the essence, suggesting that this ROI is involved in time processing. This is in line with other evidence that ascribes a prominent role for the cerebellum during subsecond (interval) time processing (Ivry and Keele 1989; Dreher and Grafman, 2002; Harrington et al., 2004; Grondin, 2008). Together, these results thus demonstrate a functional role for both the dlPFC and the cerebellum in our task. Note that voxels in the striatum showed significant activation during the decision phase across all reward schedules (Fig. 2*A*,*B*).

The PPI analysis of both dlPFC seeds indicates a modulation of neural connectivity between the dlPFC and the striatum when comparing high-threshold with low-threshold states (Fig. 3*A*,*B*; Table 2). During high(er)-threshold states (in which thresholds are adjusted for slower and more accurate decisions), effective connectivity between bilateral dlPFC and the left striatum was significantly increased compared with during lower-threshold states (Table 2). According to our connectivity hypotheses, we expected this neural interaction to be reflected in the magnitude of boundary modulation from the diffusion model as well. We calculated Pearson's correlation coefficient between estimates of the diffusion model boundary parameter and neural effective connectivity parameter (i.e., the PPI), correcting for multiple comparisons. We found a strong, positive correlation for the PPI estimates of the left dlPFC [$r = 0.8$ (16), $p < 0.0001$, two-tailed; Fig. 3*A*] and the right dlPFC [$r = 0.798$ (16), $p < 0.0001$, two-tailed; Fig. 3*B*] with the magnitude of boundary modulation (high–low threshold) of the computational model. This association between PPI estimates and boundary modulation firmly suggests that corticostriatal brain systems for the processing of accumulated evidence contribute to the observed changes in decision parameters. During lower-threshold states, effective connectivity between the cerebellum and the striatum was significantly increased compared with higher-threshold states (Fig. 3*C*). In line with our hypothesis, neural connectivity between the cerebellum and the striatum correlated negatively with the magnitude of boundary modulation [$r = -0.644$ (16), $p = 0.004$, two-tailed; Fig. 3*C*, using the same analysis direction as in the dlPFC analyses].

To further examine the relationship between condition differences in boundary parameters and brain activation, we performed a voxelwise covariate analysis with the magnitude of boundary modulation. This analysis resulted in a cluster of activation in the left striatum, in particular the left putamen [center of gravity (COG) (x, y, z), MNI152 = −24, 0, 2; size = 96 voxels; at $z = 2.4$ uncorrected whole brain]. Significance testing using small-volume correction in the same basal ganglia mask used for the PPI analysis resulted in one significantly activated cluster that partly overlaps with decision phase activity [COG (x, y, z), MNI152 = −29, −1, 5; 169 voxels; TFCE corrected at $p = 0.05$; Fig. 2*B*].This cluster showed similar activation during low- and high-threshold decision phases. Importantly, in the left posterior striatum, the clusters showed (1) covariation with boundary modulation, (2) PPI with left dlPFC, and (3) PPI with the cerebellum overlap [COG (x, y, z), MNI152 = −27, −3, −7; 32 voxels; TFCE corrected at $p = 0.05$; Fig. 4]. There were no significant whole-brain results from additional PPI analyses using other ROIs as seeds that were also activated during the decision phase (corrected for multiple comparisons; Table 3).

Discussion

We present converging evidence encompassing behavioral data, neuroimaging data, and computational modeling, which suggests that decision threshold modulation for reward maximization is instantiated through a change in effective connectivity within corticostriatal and cerebellar–striatal functional brain circuits during the decision phase, with the former being responsible for processing of accumulated sensory evidence and the latter being responsible for automatic, subsecond temporal processing.

Neuroimaging studies, along with pharmacological and lesion studies, indicate that the cerebellum is crucial for auto-

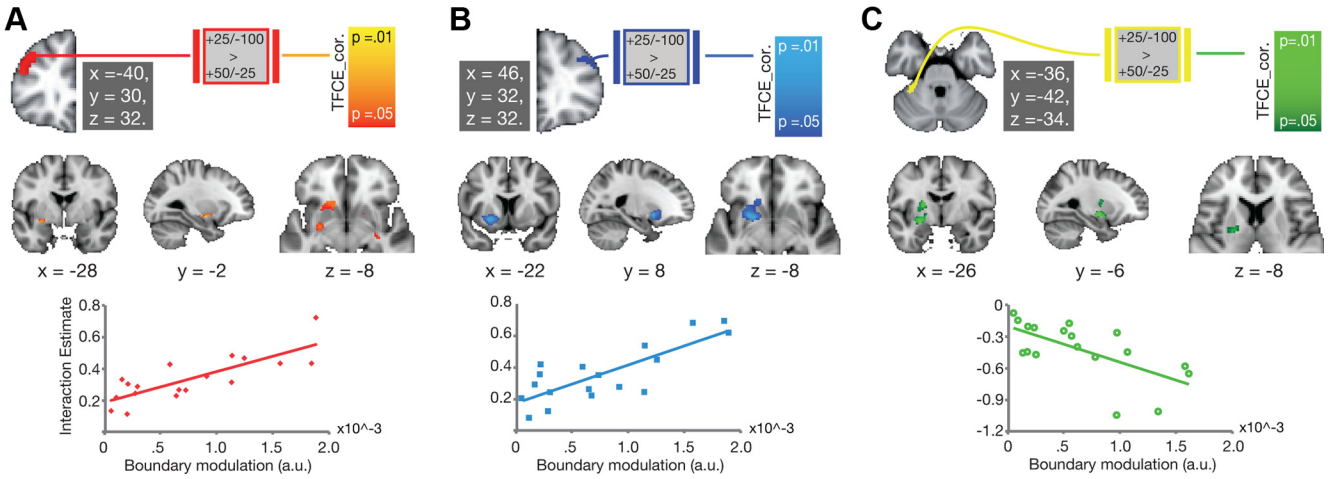

Figure 3. ***A***, From top to bottom, Left dlPFC seed ROIs, functionally interacting region of the striatum (z max = 3), association of neural connectivity parameter with boundary modulation estimate (high–low threshold states) from the diffusion model. ***B***, Same as ***A*** but for right dlPFC (z max = 3). ***C***, Same as ***A*** but for cerebellar seed, interaction with left striatal region (z max = 3.1). Blue squares, red diamonds, and green circles indicate individual subject estimates of neural interaction and magnitude of boundary modulation comparing high- with low-threshold states.

Table 2. dlPFCs and cerebellar PPI results

Seed	COG (x, y, z; (MNI152)	n voxels	z max (low threshold)	z max (high threshold)	PPI (COG, TFCE $p = 0.05$)	PPI z max (high = 1, low = −1)	n voxels (PPI)
Left dlPFC	−40, 30, 32	201	4.01	4.211	−18, 2, −7	2.989	219
Right dlPFC	46, 32, 32	51	3.93	4.264	−19, 10, −7	2.986	253
Cerebellum	−36, −42, −34	83	5.18	4.281	−24, −6, −1.6	3.131	376

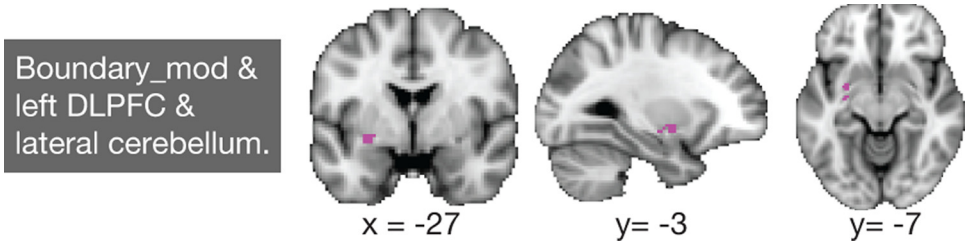

Figure 4. The clusters showing (1) a covariation with boundary modulation, (2) PPI with left DLPFC, and (3) PPI with the cerebellum overlap (COG: −27, −3, −7; 32 voxels, in pink).

Table 3. PPI results for 10 significantly activated clusters for the decision phase

Seed	COG (x, y, z, MNI152)	n voxels	z max
Paracingulate cortex	0, 20, 42	367	7.53
Right occipital cortex	40, −66, −11	108	6.47
Cerebellar cluster 1	29, −59, −53	176	5.86
Right lateral occipital cortex	42, −76, 4	76	5.62
Cerebellar cluster 2	−20, −62, −27	238	5.07
Cerebellar cluster 3	−27, −42, −32	60	4.87
Left precentral gyrus	−52, 2, 36	206	4.11
Supplementary motor area	−3, 3, 49	57	4.07
Left precentral gyrus	−32, −8, 48	73	3.79
Brainstem	5, −24, −12	52	3.66

matic subsecond temporal information processing (Ivry and Keele, 1989; Hazeltine et al., 1997; O'Reilly et al., 2008; without disregarding the ongoing debate concerning the exact role of the cerebellum in temporal processing, see Mauk and Buonomano, 2004; Coull et al., 2011). We propose that stronger effective connectivity in cerebellar–striatal brain systems places a greater weight on available decision time (corresponding to a time stopping rule; Busemeyer and Townsend, 1993; Gold and Shadlen, 2002; Cisek et al., 2009) compared with evidence accumulation during decision making. Conversely, stronger connectivity between the dlPFC and the striatum during high(er)-threshold states places a greater weight on the accumulated evidence during deliberation.

These results are generally consistent with previous empirical and theoretical accounts (Bogacz et al., 2006; Lo and Wang, 2006; Forstmann et al., 2008; Salinas, 2008; Deco et al., 2010). Notably, however, our results partly diverge from the predictions of a theoretical model proposed by Lo and Wang (2006). We observed stronger connectivity in a corticostriatal network during higher-threshold states, which leads to more accurate and slower decision making. Conversely, the biophysical network model implements strong(er) connectivity in corticostriatal pathways, producing low(er) decision thresholds for fast(er) responses with lower accuracy. Simulations of the computational model show that the optimal synaptic efficacy for reward maximization depends on task difficulty (Lo and Wang, 2006, their Fig. 7*B*,*C*). Lo and Wang show that, for more difficult choices (low motion coherence), synaptic efficacy is tuned toward higher thresholds. However, the computational model does not incorporate information about elapsed time, which is crucial for reward maximization in our task. Moreover, motion coherence was not manipulated in our experiment; in our task, more difficult choices are rather instantiated by reward schedules that entail a bigger loss and require therefore more accurate and slower decision making. Addi-

tional support for our interpretation of the observed changes in connectivity may evolve when considering the signal-to-noise ratio (SNR) in the cortex (cf. Faisal et al., 2008) and how signal gating modulates it. In the context of adaptation to stimulus quality, a theoretical analysis (Lo and Wang, 2006) suggests that the downregulation of the decision threshold is mediated by an increase of corticostriatal synaptic efficacy. This mechanism could be suboptimal in the context of changing reward schedules as we describe below.

We assume that change in synaptic efficacy is mainly instantiated through a gating process, in which stronger gating leads to weaker synaptic efficacy (cf. Salinas and Thier, 2000; Chance et al., 2002). Importantly, gating has the effect to increase the SNR because it primarily filters weaker "noise" activity (cf. Purcell et al., 2010). The underlying assumption here is that "signal" spikes have generally higher firing rates than "noise" spikes, and a low synaptic efficacy effectively filters out noise (cf. Purcell et al., 2010). Hence, increasing the synaptic efficacy by downregulating the gating process reduces the SNR. In the context of adaption to higher quality of perceptual input, for which the model of Lo and Wang (2006) was developed, this reduction of SNR is unproblematic because it is counterbalanced by the greater SNR in cortical accumulation neurons. However, when the synaptic efficacy is adjusted in the context of changing reward schedules, no counterbalancing occurs, leading to a weaker SNR of the accumulation signal sent to striatal neurons.

In our interpretation, the striatum combines evidence (dlPFC) and available time information (cerebellum) for the execution of a motor response (Middleton and Strick, 1994; Hoshi et al., 2005; Balleine et al., 2007; Cohen et al., 2009). In a nutshell, we assume that, independent of orientation toward speed or accuracy, a fixed amount of input to the striatum is required for action execution (cf. Mink, 1996) (consistent with that, we did not find that activation differed between conditions in the striatum). This input can stem from either cortical accumulation regions or from cerebellar timing regions (modulating baseline firing of the striatum). Depending on the response condition, the connectivity between accumulation and timing region on the one side and striatum on the other is adjusted. Note that both decision drivers always influence striatal activation, but the relative importance can vary. More specifically, in higher-threshold states, synaptic efficacy in a corticostriatal network should be greater and in a cerebellar–striatal network should be smaller compared with the low-threshold state. Thus, the decision threshold and the reward frequency are sensitive to the relative strength of corticostriatal and cerebellar–striatal connectivity: the greater the relative strength of the corticostriatal connectivity, the higher the threshold, and the greater the cerebellar–striatal connectivity, the lower the threshold. This mechanism can also be expressed in a simple equation, in which a vector of firing rates of striatal neurons (N_{Str}) is the weighted average of firing rates of cortical neurons (N_{co}) and cerebellar neurons (N_{ce}): $N_{Str} = \alpha \times N_{co} + \beta \times N_{ce} + x$, where x are other influences on striatal activity including noise. From this equation, it is easy to see that a change in synaptic efficacy, i.e., in the weights α and β, changes the correlation between the time series N_{Str} on the one hand and N_{co}, and N_{ce}, respectively, on the other hand. This formulation also shows that using changes in effective connectivity (as measured using BOLD fMRI) as a marker for changes in synaptic efficacy is well justified.

One interesting aspect of mechanisms for threshold adaptation is whether the observed changes in connectivity need to remain active throughout the entire task. In the mechanisms we propose, the persistent changes in connectivity represent different modes of processing under which decision making is performed in our task to maximize rewards. Persistent connectivity modulation is observed because, in every trial, sensory information and elapsed time are integrated until a decision threshold is reached (differently, depending on the reward schedule) to form a decision. Trial feedback and dependent adjustments may be additionally reflected by this persistent activity. Note that we see these persistent changes as a complementary process to processes of state resetting or switching (cf. Rushworth et al., 2002; Forstmann et al., 2008).

An alternative account of boundary modulation in the context of an urgency model or collapsing boundary model (cf. Cisek et al., 2009) is that decision boundaries collapse faster when the decision time is shorter. To investigate the plausibility of such a model, we fitted RT data to a diffusion model implementing an exponentially collapsing boundary (courtesy of Jonathan Malmaud and Antonio Rangel). However, model comparison indicates that this collapsing boundary version of the diffusion model does not improve the fit compared to a modulating boundary model. Moreover, we do not find significant correlations between the difference in collapse rate of the boundary parameter and the PPI results. Still, future work should test alternative formulations of the urgency model (e.g., comparing linear, logarithmic, or exponential collapse over time).

One potential alternative interpretation of the PPI results is the simple "reduced noise through attention" hypothesis. Subjects might pay more attention in trials with more at stake, which by reducing noise in the computations performed in all relevant areas increases the observed functional connectivity in the trials with emphasis on accuracy. However, this hypothesis is inconsistent with our result of a stronger cerebellar–striatal correlation in the low-threshold condition. Hence, the "reduced noise" argument cannot explain all our results. Moreover, if attention was the main driver of performance difference between conditions, accuracy differences should have been greater. This is because we had well-trained participants who performed the task at relatively low-coherence levels selected for 75% accurate responses in the neutral threshold condition (see Materials and Methods).

As described above, we propose that the striatum combines evidence and available time information for the execution of a motor response, which we assume to be coded in dlPFC and cerebellum, respectively. The dlPFC has been implicated in the processing of accumulated sensory evidence during decision making (Heekeren at al., 2008; Domenech and Dreher, 2010; Philiastides et al., 2011). Studies on value-based decision making locate the comparator/accumulator in the dorsomedial PFC (dmPFC) and the intraparietal sulcus (IPS) rather than the dlPFC (Basten et al., 2010; Hare et al., 2011). The distinctiveness of the implicated brain regions (dlPFC vs dmPFC) is not uncommon and is likely attributable to task and stimulus differences. Perceptual and value-based decisions share a common neural mechanism (change in connectivity), but the neural substrate can differ, even within the domain of value-based choices. For example, Basten et al. (2010) locate a cost–benefit comparator mechanism in the ventromedial PFC and the accumulator in the IPS. The general mechanism of difference-based accumulation of evidence is the same as in the study by Hare et al. (2011) but the neural substrate differs. Future research based on single or multiunit recordings and/or high-resolution fMRI will be required to

clarify the invariance of mechanisms and regions that are involved in these decision-making processes.

In conclusion, we present converging evidence from behavioral data, neuroimaging data, and computational modeling showing that threshold adjustments to maximize net reward are instantiated through a change in effective connectivity within corticostriatal and cerebellar–striatal brain systems. Our findings on the neural mechanism of decision threshold modulation could be highly relevant for the understanding of neuropsychiatric disorders that are accompanied by impulsivity and or inflexibility (Mulder et al., 2010) and how temporal information can be used to inform decision making (cf. Hanks et al., 2011).

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Research Project 2.

Nikos Green, Rafal Bogacz, Julius Huebl, Ann-Kristin Beyer, Andrea A. Kühn, and Hauke Heekeren (in revision). **Deep Brain Stimulation of the STN reduces the influence of conflict in perceptual decision making.**

Deep brain stimulation of the STN reduces the influence of conflict in perceptual decision making.

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Summary

Making the correct decision at the right time is a pivotal aspect of behavior. Neurocomputational models of optimal decision making ascribe a crucial role - the computation of conflict between choice alternatives - to the subthalamic nucleus (STN) [1-5]. Specifically, these models predict that deep brain stimulation (DBS), which disrupts information processing in the STN, will diminish the influence of decision conflict on decision making under high conflict [2, 4, 6]. We asked patients with DBS implants to judge the direction of motion in random dot stimuli [7] under different states of DBS. The trials differed in difficulty (motion coherence) and response instruction (fast or accurate) leading to increased RTs in trials with higher task difficulty in healthy subjects. Results indicate that DBS significantly influences a) performance for perceptual decisions under high decision conflict, as well as b) the magnitude of decision criterion adjustment. In particular, when DBS was turned on, the influence of task difficulty on RT was significantly reduced and a race model best accounted for observed data. In contrast, when DBS was turned off, RTs increased substantially as the task became more difficult and a diffusion model best accounted for behavioral data. Individual data fits of evidence accumulation models demonstrate different information processing under distinct DBS states. Together these findings suggest a crucial role for the STN in adjusting decision making during high-conflict trials in perceptual decision making.

Highlights

- DBS of the STN reduces the influence of decision conflict in perceptual decision making
- DBS of the STN changes the magnitude of decision criterion modulation.
- Comparison of fits to different evidence accumulation models suggests altered information processing during DBS.

Results

Cortico-basal ganglia (BG) networks control the expression of competing response alternatives and mediate decision making [1, 6, 8-11]. A central role in cortico-BG network computations for decision making is ascribed to the subthalamic nucleus (STN) [2, 4, 6, 12-15]. The STN receives input from the frontal cortex via the hyperdirect pathway and from subcortical regions via the indirect cortico-BG pathway and reciprocal subcortical connections [16]. The STN is integrated in parallel motor and non-motor cortical-BG thalamic loops [17] and distinct motor, limbic and associative subterritories have been identified [18]. As a consequence, STN activity efficiently regulates the expression of actions [12, 13, 19] as well as executive processes such as decision making [6, 15]. Modulation of STN activity – using DBS- may influence cognitive, motor and limbic circuits at the same time [14, 20-22]. Recently it has been suggested that the STN computes conflict between choice alternatives and mediates decision making accordingly [2, 23]. Bogacz and colleagues [3, 4] advanced this approach theoretically by demonstrating how cortico-BG networks that provide conflict computation through the STN can implement an optimal decision-making procedure, the Multihypothesis Sequential Probability Ratio Test (MSPRT) [24]. In this procedure, sensory evidence is accumulated only as long as it is necessary to gain a required level of confidence. Thus, MSPRT is thought to minimize the decision time for any specified level of accuracy [5, 24-26]. In the MSPRT model, information regarding the activity of sensory neurons selective for rightward motion affects the activity of neurons selective for leftward choices via the STN and vice versa (Figure 1A and 1B). The model predicts that the disruption of the STN using DBS will make the activity of neurons selective for left choices more independent from sensory neurons selective for rightward motion. Furthermore,

because STN neurons are the only highly non-linear neurons in the MSPRT model, silencing of the STN in the model results in activities of neural populations in the final stage of the model that are linearly proportional to the integrated evidence for corresponding alternative (Figure 1C). Hence, in this framework, the disruption of STN activity using high frequency DBS curtails conflict computation and should therefore fundamentally change how available information is used to form simple perceptual decisions (Figure 1A, B, C, see Supplemental Experimental Procedures for details). For instance, it has been shown that MSPRT can (Figure 1A) be implemented by a drift diffusion model (DDM, Figure 1B) [3-5, 26]. The DDM achieves the most efficient computation by integrating the difference between the accumulated evidence supporting the two alternatives and determines the decision processes as soon as this difference exceeds a certain threshold (Figure 1B). The implementation of the MSPRT by cortico-basal ganglia networks requires specific computational functions of the STN, i.e. the computation of conflict [3-5]. This follows previous theoretical considerations and empirical results that show that the STN mediates decision making [3, 5, 6, 15, 23, 26]. DBS inhibits this specific function and results in premature or impulsive decision making [8, 18]. It thus follows that under normal STN functioning a diffusion model should best describe RT decision data [2, 3, 6, 26]. On the contrary, under impaired STN computation such as during DBS, the RT data should be best described by a suboptimal simple choice model such as the race model as it does not integrate the conflict between alternatives [2, 3, 6, 15, 26]. In summary, neurocomputational models predict that DBS applied to STN should decrease the effect of conflict on RTs during perceptual decision making [2, 3, 6, 26].

We combined psychophysical experimental methods (Figure 2) and computational modeling (Figure 1 and Supplemental Information) to test this algorithmic theory of cortico-basal ganglia computation for optimal decision making [3-5].

BEHAVIOR

With increasing coherence, participants were faster (main effect of stimulus coherence: $F(5,35) = 165.157$, $p < 0.001$) and more accurate ($F(5,35) = 451.842$, $p < 0.001$, Figure 3A, 3B). This is not surprising, as with lower stimulus coherence, the sensory information is more conflicting and the task is more difficult.

Computational models of cortico-BG networks predict that DBS reduces the effect of conflict during decision making [2, 3]. Indeed, the rate of change in RT as a function of coherence was lower when DBS was turned on than when it was turned off in the accuracy condition (Coherence * DBS: $F(5,35) = 24.182$, $p < 0.001$; Coherence * DBS * Instruction, $F(5,35) = 9.219$, $p < 0.001$, Figure 3B). There was also a similar but weaker effect on the slope of accuracy as a function of coherence. This slope was less steep when DBS was turned on than when it was turned off during the accuracy condition (Interaction: Coherence * DBS, $F(5,35) = 4.419$, $p = 0.003$; Coherence * DBS * Instruction, $F(5,35) = 9.219$, $p < 0.001$, Figure 3A). Under the speed instruction, the participants had lower mean RTs (main effect of Instruction: $F(1,7) = 135.039$, $p < 0.001$) and lower accuracy ($F(1,7) = 114.701$, $p < 0.001$, Figure 3A, 3B) compared to the accuracy instruction condition. The effect of instruction on RT was greater for low coherence than for high coherence trials (Coherence*Instruction: $F(5,35) = 15.345$, $p = 0.001$). This result was expected because RTs were longer overall during low stimulus coherence. DBS appeared to affect the patients' overall response profiles, i.e., patients on DBS were faster (main effect of DBS: $F(1,7) = 85.18$, $p < 0.001$) and less accurate ($F(1,7) = 120.627$, $p <$

0.001) compared to testing with DBS turned off. The effect of instruction was greater when DBS was turned off than when it was turned on (DBS * Instruction: F (1,7) = 6.329, p = 0.04). DBS of the STN resulted in diminished the effects of conflict on both the reaction time (RT) and decision accuracy in perceptual decision making (Figure 3), indicating that STN function is central to sensory-based action selection. Participants with DBS were tested against a group of age-matched controls (see experimental methods and supplementary material) as a considerable influence on behavior could be related to PD motor deficits with abnormal dopaminergic processing. Note that all of our patients were on dopamine medication and the comparison between control and PD patients indicates a pattern that in in line with the our hypotheses (see Supplemental Information for details). Control subjects did not differ in RT from patients under DBS or without DBS during the speed condition (Figure 3A, upper panel). However, control subjects differed significantly in RT from the patients under DBS during the accuracy condition for the 3 lowest coherence levels (RT (controls, DBS_OFF) > RT (DBS_ON, see upper panel of Figure 3B). Control subjects did also differ in accuracy from patients under DBS on those low coherence / high conflict trials during the accuracy condition (AC(control, DBS_OFF) > AC(DBS_ON), see lower panel of Figure 3B). Moreover, under low conflict (the two highest coherence levels) control subjects were significantly better in AC from both DBS samples in both accuracy and speed conditions (Figure 3A and 3B lower panels right part of both graphs). Taken together these results are in line with previous empirical findings in that DBS impairs the ability to adjust decision making by modulating the decision threshold under high conflict [2, 6, 15, 27-29].

These results indicate a) that participants' behavior is comparable to that of healthy participants (i.e. during the speed instruction) and b) that DBS of the SNT leads to a

computational silencing of the conflict function during decision making as shown in decision behavior during the accuracy instruction, in which the conflict between alternatives requires the slow down of the decision process. These findings are in line with a recent study that investigated the influence of DBS and dopamine medication in a) a comparable patient group and b) applying a similar computational model [30. In that study, patients were tested on a memory and a probabilistic choice task. It was shown that DBS specifically impairs probabilistic evidence integration whereas dopamine medication solely improves memory for learned response associations [30].

MODELING

Next, we fitted various MPSRT-derived versions of the race and diffusion model to individual RT datasets (see Supplemental Information). As predicted, a diffusion model account better described the behavioral data when DBS was turned off, whereas a race model account better described the behavior under DBS (cf. Figure 1, and Supplemental Table 1). These model fits were additionally tested against a variety of other models in each individual dataset and are in agreement with the predictions of the theoretical model of Bogacz and Gurney [3]. The relative quality of the model fits to RT and ER was assessed by using the Akaike information criterion (AIC) [31]. The combined model (race account for describing DBS ON data and diffusion account for describing DBS OFF data) is clearly preferred according to the comparison to all other models in 6 out of 8 subjects (Table 1). In two cases the combined model has similar AIC values as a model assuming a change in signal parameters across DBS conditions. In this case we cannot distinguish the models based on the AIC value, the quality is the same, indicated also by the Akaike weights (Supplementary Table 2), which give the weight of evidence (between 0 and 1) in

favor of each model. Figure 4, depicts the experimental data during DBS OFF alongside the estimated model fits of the DBS OFF diffusion model and the baseline model (in which parameters were estimated across DBS conditions, see Supplement). It is clearly observable that the DBS condition specific version of the diffusion model fits the data better than a basic model.

Finally, to test the effect of DBS on thresholds we extended our models by estimating a so-called conflict model that implements separate thresholds for low conflict and high conflict trials (low conflict: 1.6%, 4.8 and 8 % and high conflict: 12.8, 20.8 and 51.2 % stimulus coherence). The AIC values do not distinguish the initially used diffusion model (with threshold parameters across coherence levels) from the conflict model (see Table 2). It is informative to compare threshold differences from the conflict model in order to test whether thresholds are affected differently in high conflict trials compared to low conflict trials. The results show that the threshold difference for the low coherence trials is smaller than for the high coherence trials: $t(7) = -3.9002$, $p = 0.0059$; Table 3). This result is in line with our hypotheses that DBS affects modulation of decision making specifically under high perceptual conflict.

Discussion

Theoretical accounts of brain processes are important because they can provide testable predictions about the functionality of specific neural systems during brain functions such as for example decision making. Our behavioral and modeling results reveal a significant effect of DBS of the STN regarding the accuracy and RT for high conflict, low coherence direction of motion judgments. These results are in agreement with previous empirical studies as well as theoretical models that ascribe a crucial role to the STN during decision making, especially during high-conflict conditions [2, 6, 15, 23, 25, 27, 28]. Importantly, the present study extends previous

empirical findings [6, 15, 27-29] to the domain of perceptual decision making while at the same time supports computational models of decision making based on the statistically optimal MSPRT. It has been shown that MSPRT presents a framework for optimal decision making [32, 33]. This property of optimality has been analytically demonstrated for accuracy levels approaching 100% [25]. In simulations with lower accuracy, MSPRT achieved faster or equal decision times compared to simpler procedures [33]. Our modeling approach empirically tests this algorithmic framework. Individual behavioral datasets are well described by race and diffusion models accounting for changes in information processing in the STN under different DBS conditions, as predicted by the MSPRT model of cortico-BG network computations. These results strongly support the assertion that cortico-BG networks implement system-level computations that optimize decision making for specific forms of simple decision making. Importantly, our findings also support the view that the STN performs crucial computations on conflict between choice alternatives during sensory based decisions. Modeling results, especially the estimates of the decision threshold parameter, indicate that the integration of decision conflict has a strong STN dependence. Our findings indicate that DBS influences the ability to adjust the response threshold when required to adjust decision making for accurate decisions, albeit under high conflict. When comparing the magnitude of decision threshold parameter adjustment between different amounts of conflict under DBS conditions (Table 3 and Supplemental Figure 2) it becomes evident that the STN mediated computation of decision conflict is used to adjust decision making. This is in line with previous work showing that the STN influences the decision threshold online by modulating cortico-basal ganglia communication by exerting control over basal ganglia output nuclei [6, 15, 23]. Oftentimes we face a trade-off between deliberation

time and evidence accumulation [26, 32]. Depending on the circumstances being fast offers the potential for higher reward. However, slow decision making increases accuracy. The ability to modulate the decision threshold is thus crucial in order to set this trade-off effectively, for example during changes of internal and external circumstances [6, 34, 35]. The MSPRT model itself is silent about the speed-accuracy tradeoff (SAT), because it does not describe how this tradeoff is controlled. To make any predictions on STN activity using the MSPRT model, one has to assume a particular mechanism for controlling the tradeoff. If one assumes that the tradeoff is controlled by the increase in the baseline activity with speed emphasis, then indeed the activity of STN in the MSPRT model before stimulus onset would be higher in the speed that the accuracy condition [3, 4, 26]. However, please note by the end of the choice process the expected STN activity would be similar in the speed and accuracy conditions, and the STN would modulate the decision process for longer in the accuracy than speed condition. Therefore, the disruption of STN affects the RTs in the model to a larger extent in the accuracy than the speed condition. Moreover, in the MSPRT model, the STN activity is a function of activity of the integrators rather than of the sensory input directly [3]. Please note that in each coherence condition, the activity of integrators will traverse similar range of values i.e. from baseline to threshold, so the STN will also have similar range of activities in different coherence conditions. However, in the low coherence conditions, reaction times are longer, so that the STN affects decision process for longer, thus its disruption has larger effect on reaction times.

In this study, especially for high conflict, low motion coherence decisions, the top-down mechanism implementing response instruction based adjustment of decision

making appears to be too weak to overcome the automatic bottom-up computations of the basal ganglia network [13] under DBS stimulation. This is in line with another study [36], in which the application of a race to threshold model to RT data from a DBS sample leads to the interpretation that DBS of the STN a) amplifies the descending cortical signals to the motor output structure and b) reduces the tonic background inhibition that suppresses unwanted premature responses through DBS.

It may seem surprising that (as shown in Supplemental Figure 2) each model fits the data from both conditions relatively well (e.g. the race model can relatively well reproduce the steep dependence of RT on coherence in DBS off condition and more shallow dependence in the DBS on condition). This is a result of the model being fitted with a separate set of parameters for each condition (so for a different sets of parameters the race model may produce more or less steep dependence of RT on coherence). This illustrates the importance of considering different models of information processing to compare different states [37, 38].

The STN is comprised of different subterritorries that are involved in parallel cortico-BG loops [18, 39]. These circuits process distinct information based on a distinct topographical organization for cognitive (ventral), emotional (medial) and motor (dorsal) loops [18, 21]. Spread of current during chronic DBS to non-motor subterritorries may contribute to changes in executive processing such as decision making [40-44] or processing of affective information [45, 46]. For instance, DBS of the STN elicits premature or impulsive decision making and reduces the ability to adjust decision making, especially during highly conflicting choices [6, 15, 23]. Thus, we assumed a negative ('computation silencing') effect rather then a normalizing effect under DBS. We derive our hypothesis that suggests that high frequency DBS

of the STN, has adverse effects on conflict computation from theoretical and empirical results. First, in the cortico-basal ganglia model of optimal decision making, a central function for the computation of conflict is ascribed to the STN [2, 3, 6, 9]. This has been corroborated by empirical results such as for instance recordings of STN activity [15, 18]. Second it has been empirically shown that DBS of the STN reduced the ability to adjust decision making [6, 23, 28]. Taken together, we inferred that although DBS of the STN significantly improves tremor, rigidity, akinesia, or gait, DBS of the STN at the same time impairs other functions served by the STN, for example decision making. Indeed, DBS of the STN has been shown to eliminate abnormal rhythmic oscillation thought of causing the motor symptoms in the parkinsonian state [47, 48]. Moreover, research findings support the notion that the net effect of DBS is to increase the firing of neurons, which would indeed drive the output structures of the basal ganglia and lead thereby to premature responding and thus reduced modulation of decision making [8, 11, 12, 19]. Additionally, our results are supported by the comparisons between a control group and our DBS sample (see Behavior section and Supplemental Information).

In summary, we show for the first time that STN computations on decision conflict are crucial during perceptual decision making. Using a combination of psychophysics, neurostimulation (with DBS) and computational modeling reveals that the STN is crucial for the adjustment between fast and accurate decision making in order to balance deliberation and evidence accumulation [31, 35, 49]. We present empirical evidence in support of formal models that suggest cortico-BG network capacity for optimal computation of decision making under high conflict.

Experimental Procedures

Detailed description of experimental procedures, data analysis, and computational modeling can be

found in detail in the Supplemental Information.

Participants

10 PD patients (two females, mean age: 57.3 +/- 5.2 years) with bilaterally implanted DBS electrodes in the STN were recruited during their annual consultation in the outpatient clinic at the Charité, University-Medicine Berlin, Department of Neurology, Campus Virchow, Germany (Supplemental Table 3). All patients had normal or corrected-to-normal vision, were on stable, individually prescribed PD medication and on effective subthalamic high frequency stimulation. Patients were briefed on the experiment and the nature of the employed methods. All participants gave informed consent to participate according to a protocol approved by the local ethics committee. We also tested an age matched control group (9 subjects, 4 females, mean age 55.2, +/- 6.03 years).

Task

Participants were asked to perform a two-alternative forced-choice perceptual judgment task while their stimulator was turned on or off. Participants judged whether the net motion of a dynamic random dot stimulus was directed towards the left or right (see Figure 2) and received response instruction specific per trial and per block feedback.

Data Acquisition, Analysis and Modeling

Complete datasets from 8 patients who participated throughout the entire length of the experiment were included in the analysis. All reaction times, except for those collected on missed trials and fast guesses (RT < 250 ms.), were included in the statistical analysis. We calculated in total 2 full-factorial ANOVAs: one on reaction time (RT) and one on accuracy (AC). Each 3-way repeated measurement ANOVA (rmANOVA) includes both speed and accuracy conditions and thus 24 data points (2 instructions x 2 DBS conditions x 6 coherence levels). Since we had included in our study patients that were on continuous DBS for a variable time period (1-8 years), we refrained from correlating UPDRS-III scores to the modeling results.

The collected data contains too few data points per condition to fit distinct RT distributions. Unfortunately, it was experimentally not possible to obtain more data points, as we had to adhere to ethical standards and keep the duration of the experiment at an appropriate duration for the patients, especially in the DBS OFF condition. Therefore, due to the small number of trials for each participant per condition we fitted the computational models to the error rates (ER) and mean RT for each condition (but see Supplemental Experimental Procedures for details).

Due to the limited number of data points to which we were fitting each model, we followed the approach of Ditterich [50, see also 26]: i.e., maximally constrain the race and diffusion models and fit them with as few parameters as possible. We ignored any variability in the parameters (drift, starting point and non-decision time) present in the full diffusion model (see Supplemental Experimental Procedures).

Supplemental Information

Supplemental Information accompanies this paper.

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Figure legends, and Tables.

Figure 1. Computational architectures for models of binary decision making.

(A) The diffusion model implements the sequential probability ratio test (SPRT) [30, 31].

The black and gray circles denote neural populations selective for movement toward the left and right, respectively. Labels next to the populations denote the brain areas where they are located ("Integrators" denotes cortical integrator neurons, "Output" denotes the output nuclei of the basal ganglia: the internal segment of the globus pallidus and the substantia nigra pars reticulata). The arrows denote excitatory connections, and the lines ending with circles denote inhibitory connections. The labels above and below the models indicate the values of inputs and outputs, respectively. The labels x_T^L and x_T^R denote the activities of sensory neurons selective for motion towards the left and right, respectively, at the current time T. In panel C, f is a monotonic function equal to $f(s) = -$

log(1+exp(-*gs*)), where *g* is a positive model parameter and s the sum of the difference between both alternatives for each output unit.

(B) In the diffusion model, the difference between sensory inputs for the two alternative choices is integrated. A choice is made once this integrated difference exceeds a decision threshold. Only the difference between sensory inputs affects the values of the integrators;

(C) The simplest model of binary choice is the race model. Two independent integrators accumulate sensory evidence supporting each of the two choice alternatives (here, motion to the left or right). A choice is made once the activity of any integrator exceeds a fixed threshold.

Figure 2. Experimental design

(A) Accuracy instruction emphasizing accurate responses.

(B) Speed instruction emphasizing fast responses**.**

Judgments were made in blocks of 20 trials randomly distributed over 6 levels of motion coherence (1.6, 4.8, 8, 12.8, 20.8 or 51.2 %) with speed or accuracy response instructions given at the beginning of each block for a total of 240 trials per DBS condition. In each trial, participants had up to two seconds to respond. Either a response or the deadline terminated a trial. Participants received immediate feedback on each trial.

Figure 3. Behavioral Results of patients and controls.

(A) Mean RT (top panel) and mean accuracy (lower panel) as a function of stimulus coherence during speed condition.

(B) Mean RT (top panel) and mean accuracy (lower panel) as a function of stimulus coherence during accuracy condition.

Blue lines indicate DBS_ON sample, broken black lines indicate control sample (shaded grey areas represent standard error of the mean of control sample; red lines depict DBS_OFF sample.

Error bars represent standard error of the mean (blue: DBS_ON; red: DBS_OFF). Stars indicate a significant difference between controls and PD patients on the axis of the specific coherence level.

Figure 4. Experimental data and simulated model data for DBS OFF condition. The DBS condition specific diffusion model (in green) fits the experimental data (in black) better than the baseline model

(in brown). Left side: RT; Right side: AC.

Subject / Model	1	2	3	4	5	6	7	8
Basic model	-204,96	-180,10	-221,11	-181,32	-202,26	-192,55	-183,89	-197,85
Combined	-230,10	-219,89	-240,84	-234,93	-217,75	-213,56	-221,79	-220,24
Signal_variation	-230,16	-219,87	-229,64	-231,93	-207,05	-204,39	-217,92	-210,80
Signal_constant	-220,97	-206,90	-221,30	-225,45	-211,38	-203,73	-201,75	-206,13
Threshold_variation	-221,91	-208,98	-228,90	-227,84	-215,53	-202,15	-202,36	-208,04
Threshold_constant	-228,70	-210,44	-236,44	-231,05	-204,92	-207,67	-217,89	-211,03
T0 variation	-204,07	-187,06	-228,64	-212,66	-206,40	-190,96	-193,20	-204,51
T0 constant	-220,15	-215,80	-228,46	-229,24	-206,17	-203,91	-215,50	-208,50

Table 1. AIC values of different models describing information processing under distinct DBS states (see Supplement for details). The table lists the AIC values for the BASIC model (all parameters equal across DBS conditions) and the combined RACE / DIFF model (Race for DBS_ON and Diffusion for DBS_OFF). For each subject, the AIC value indicates a better fit (lower AIC value) for the combined model than the basic model.

Subject / Model	1	2	3	4	5	6	7	8
Conflict	-126,68	-116,02	-123,72	-119,07	-113,11	-123,63	-118,97	-124,78
DIFF_ON	-125,44	-115,12	-122,82	-118,85	-113,00	-122,31	-119,56	-124,56
dAIC	1,24	1,10	0,90	0,22	0,11	1,32	0,59	0,22

Table 2. AIC values for the conflict model and the initial version of the diffusion model for the DBS_ON condition. The AIC values do not separate the model in terms of relative quality; a deltaAIC (dAIC: AIC (best model) – AIC (current model)) score below 2 indicates basically equivalent quality in explaining the data.

Subject	HIGH CONFLICT	LOW CONFLICT
1	0,100	0,151
2	0,096	0,141
3	0,078	0,113
4	0,086	0,090
5	0,072	0,114
6	0,086	0,127
7	0,035	0,039
8	0,018	0,022
MEAN	*0,071*	*0,100*
STD	*0,029*	*0,047*

Table 3. This table shows difference in decision thresholds between speed and accuracy conditions for high and low conflict trials during the DBS condition

Figures

Figure 1.

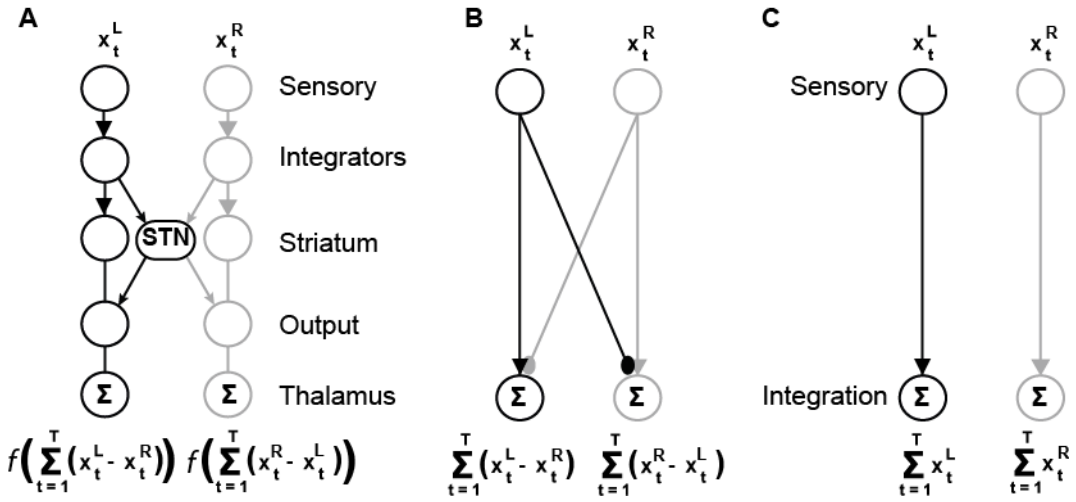

Figure 2.

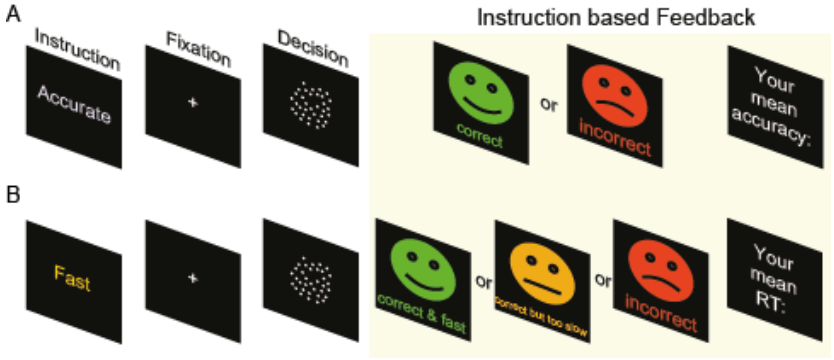

Figure 3.

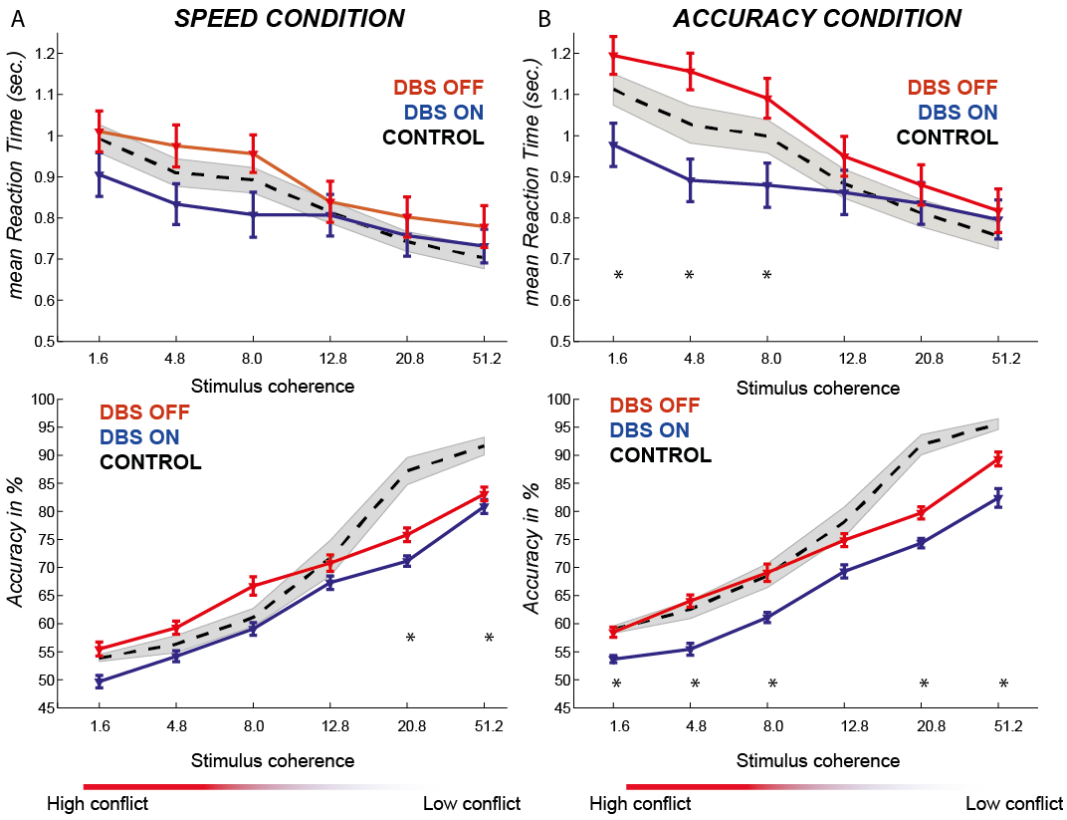

Figure 4.